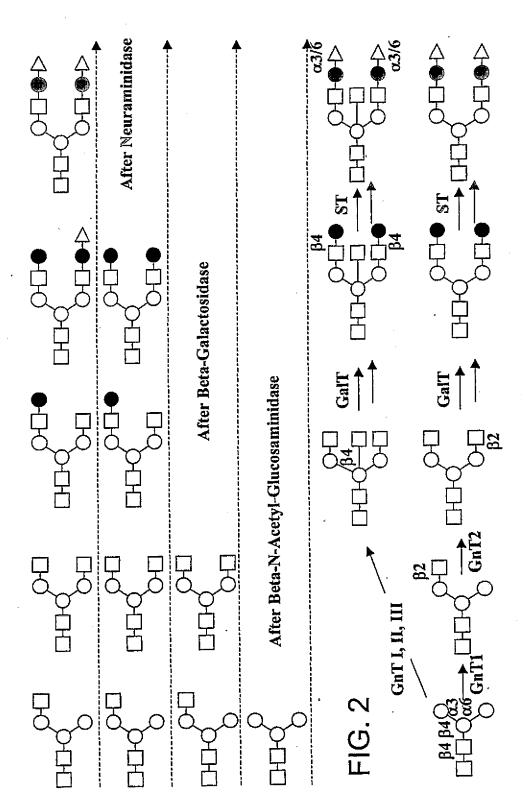
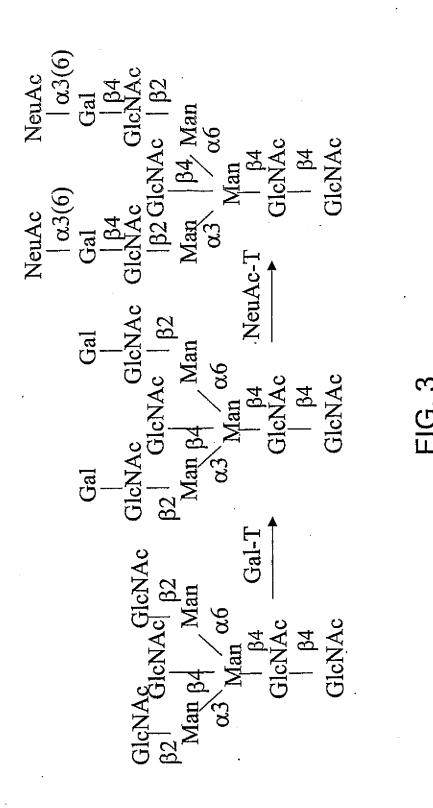
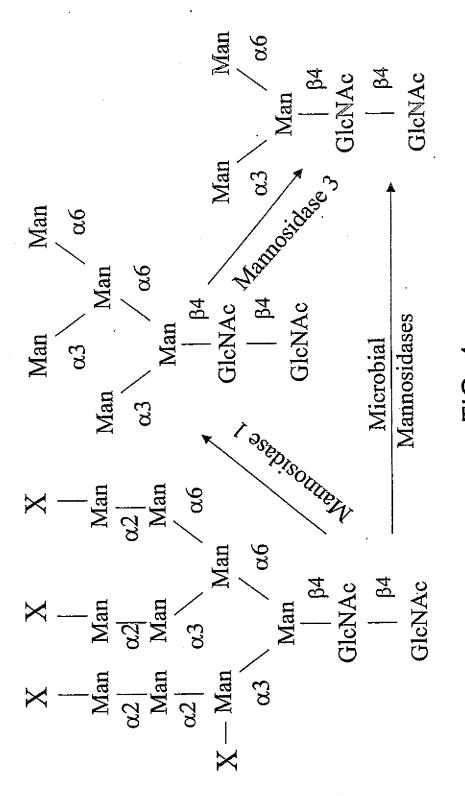


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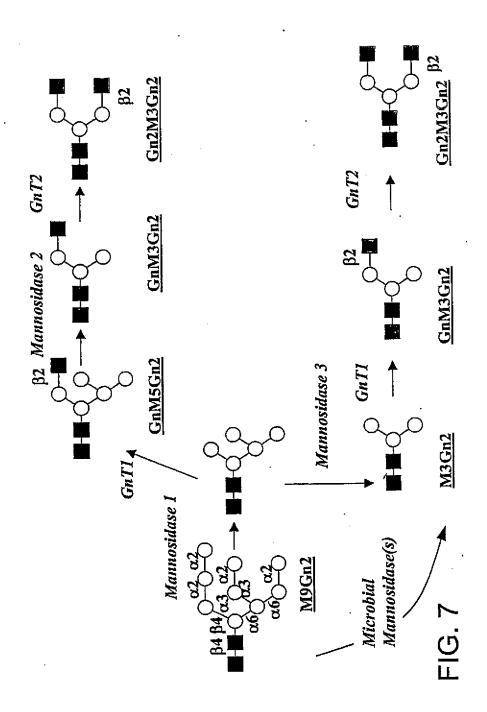


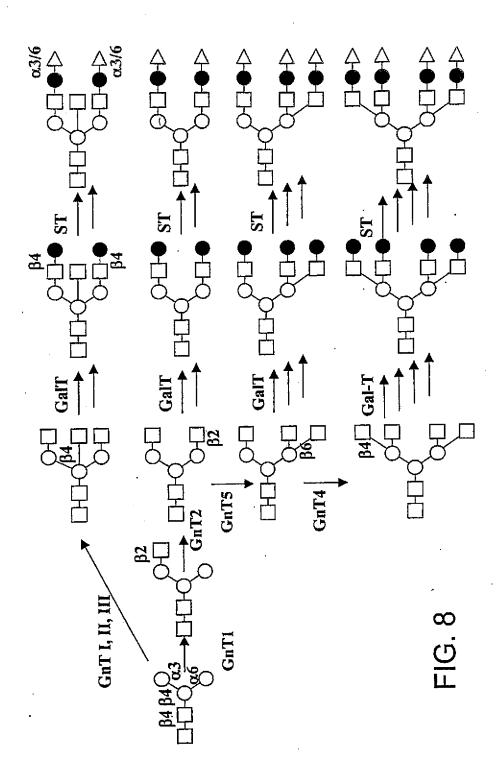




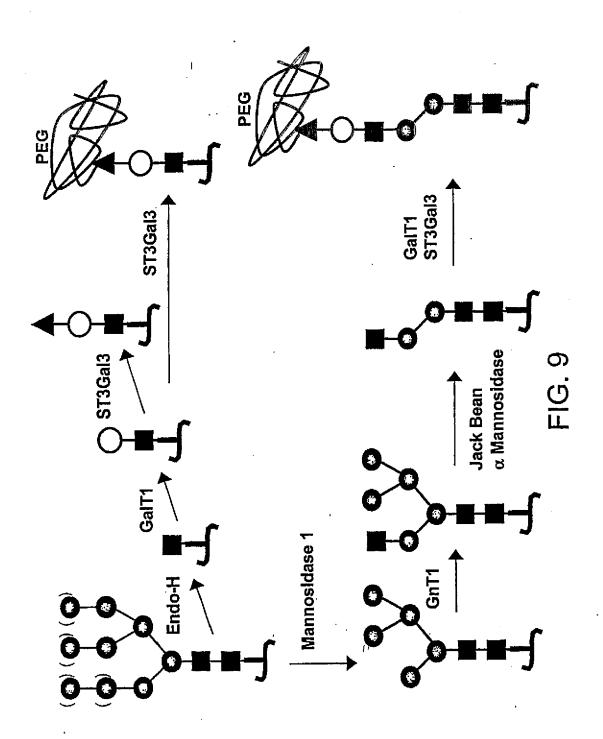
<u>-</u>G. 4

$$(GlcNAc) \qquad (GlcNAc) \qquad (GlcNAc) \\ \beta 2 \qquad \qquad | \beta 2 \qquad \qquad | \beta 2 \qquad | \beta 2 \qquad | \\ Man \qquad \alpha 3 \qquad Man \qquad (Man) \\ Xyl \xrightarrow{\omega 3} Man \qquad \alpha 6 \qquad \alpha 3 \qquad \alpha 3 \qquad \\ GlcNAc \qquad \qquad GlcNAc \qquad \qquad (Fuc)^{-\alpha 3} \qquad (GlcNAc) \qquad (Gl$$

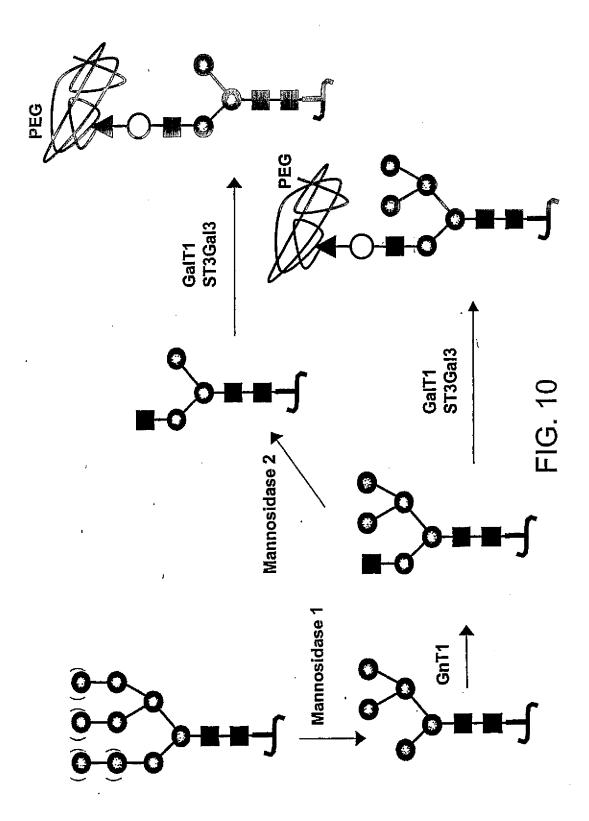


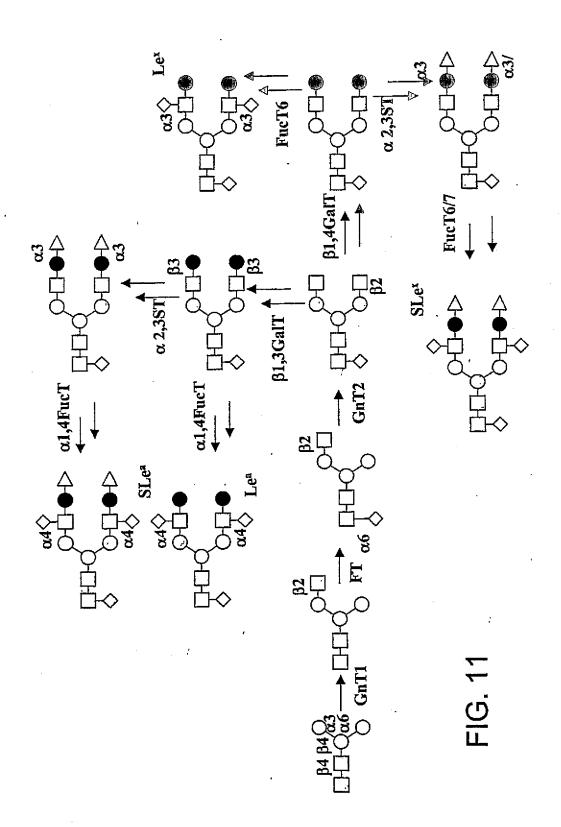


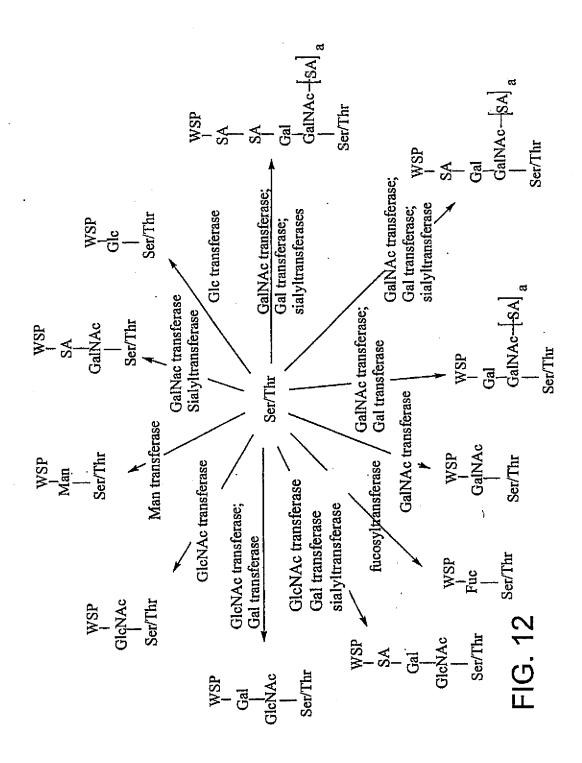
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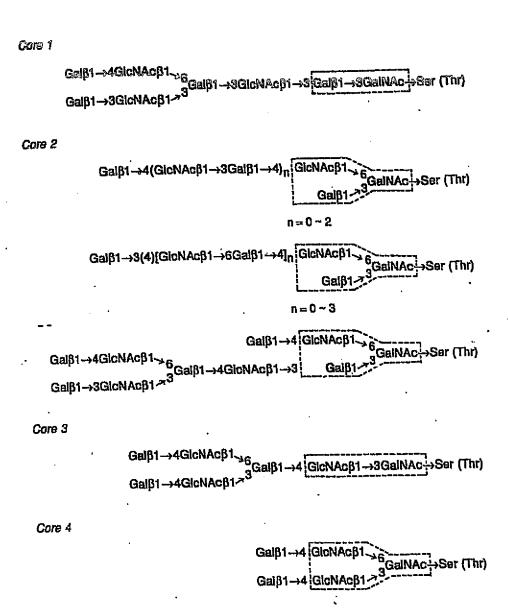
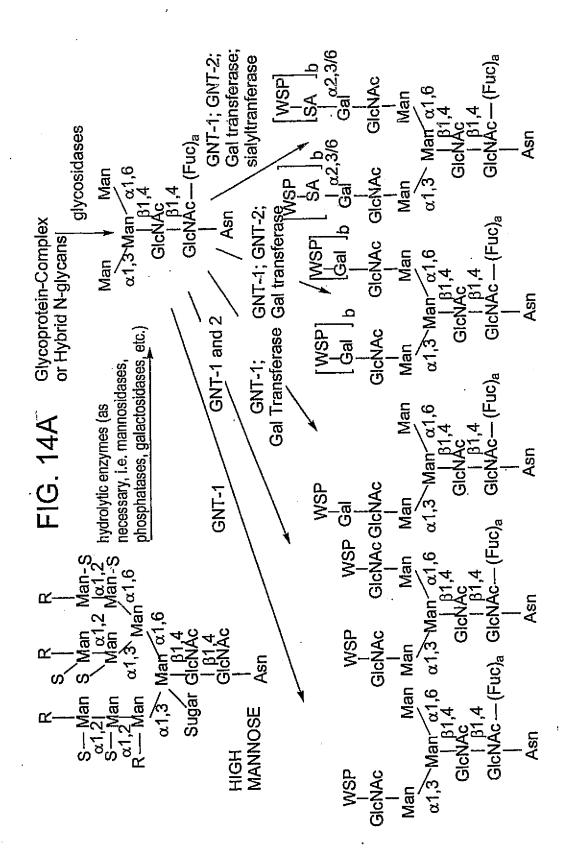
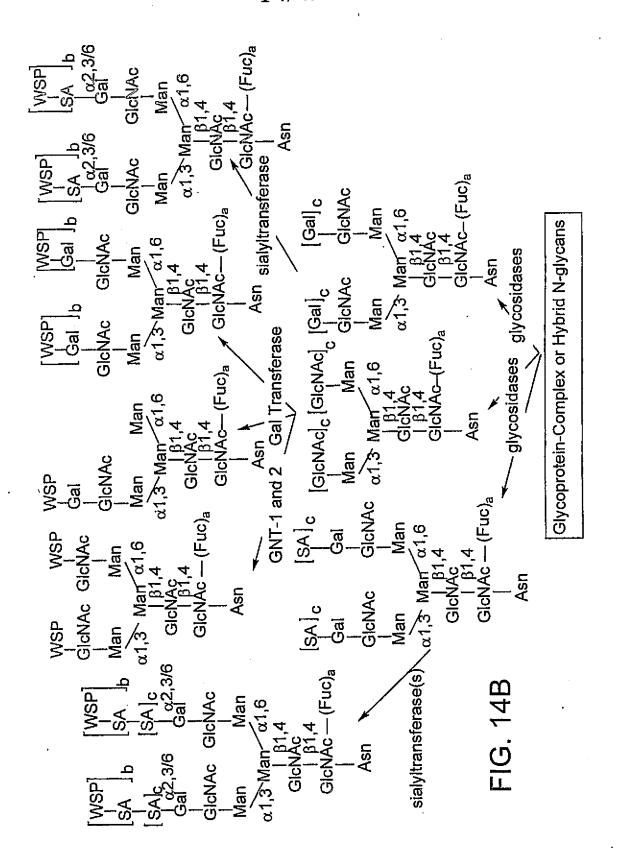


FIG. 13





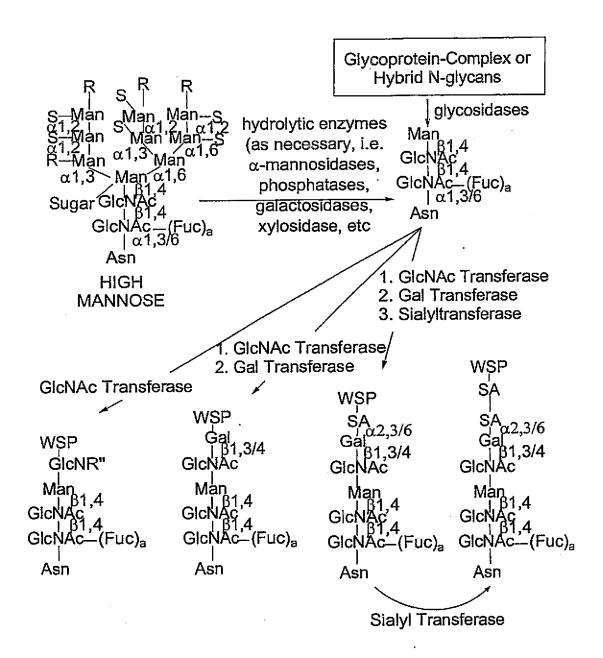


FIG. 15

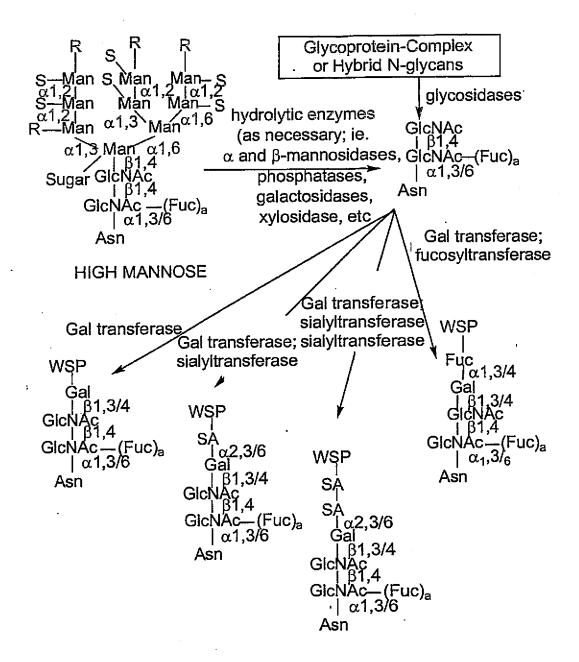


FIG. 16

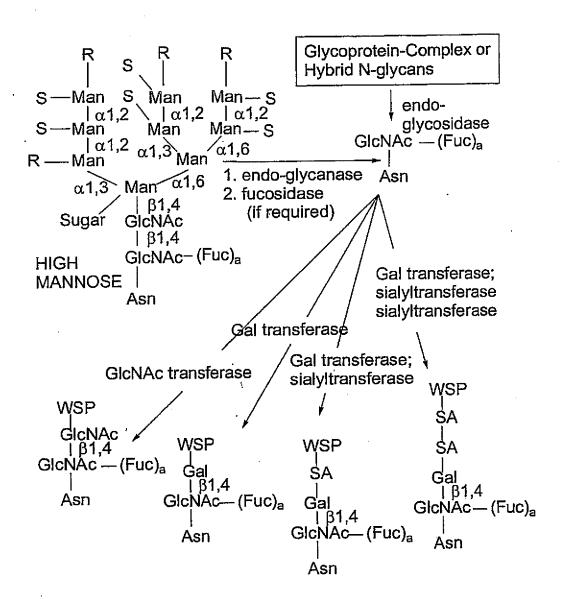
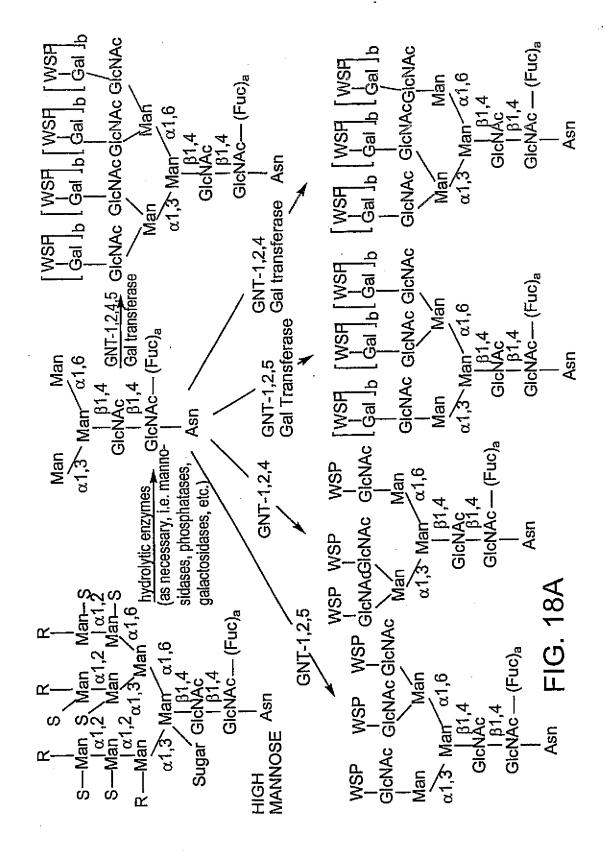
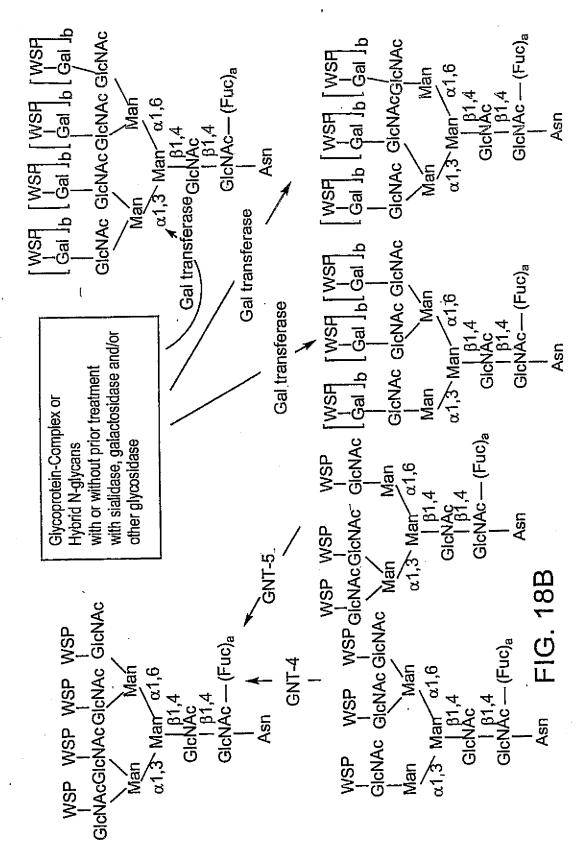
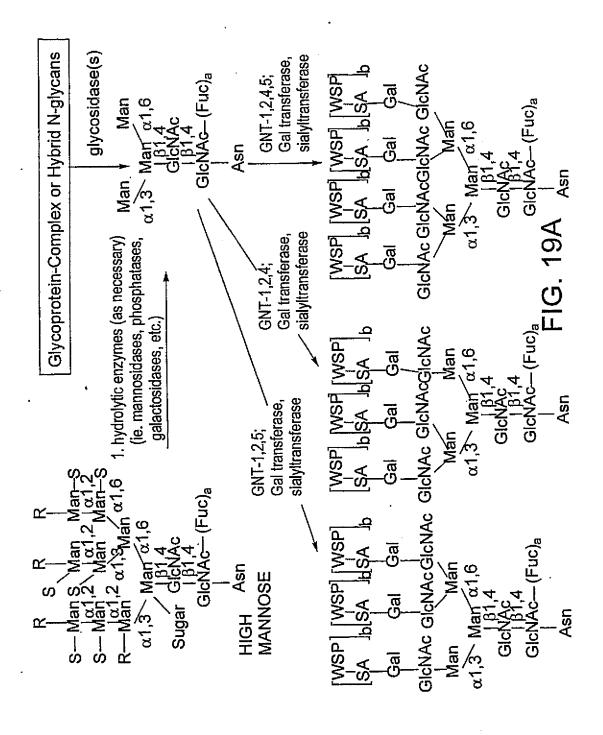
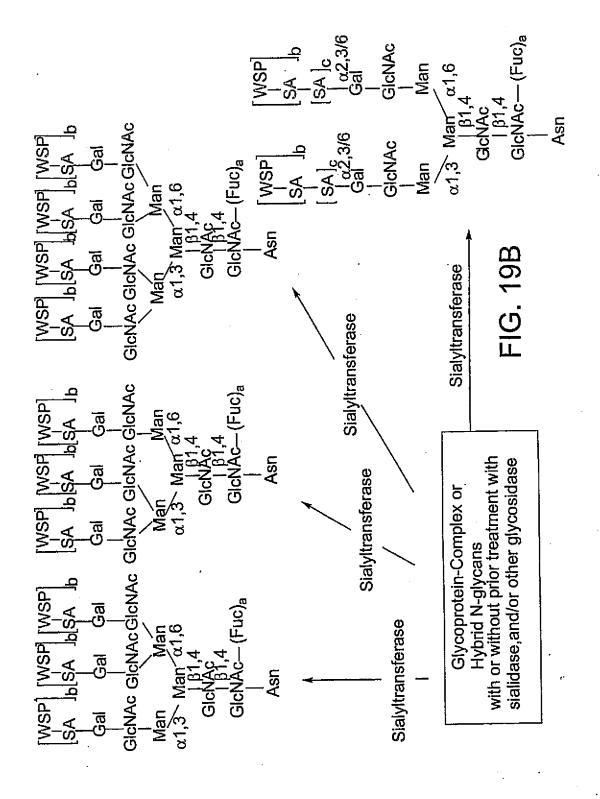


FIG. 17









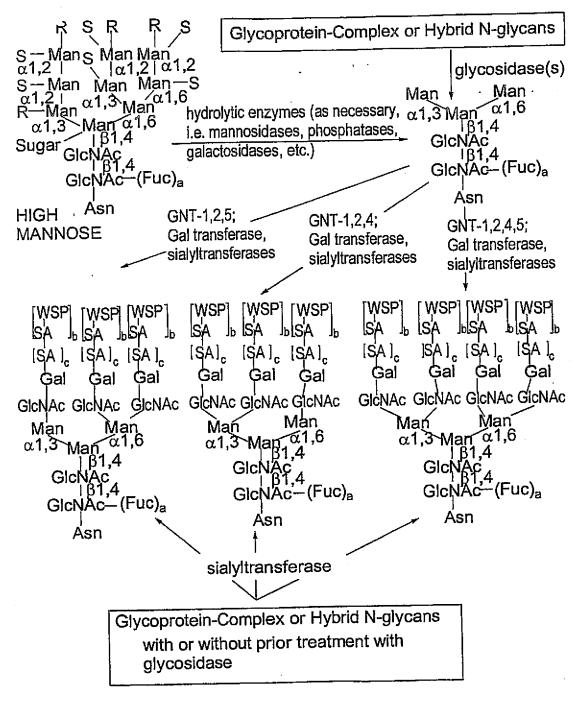
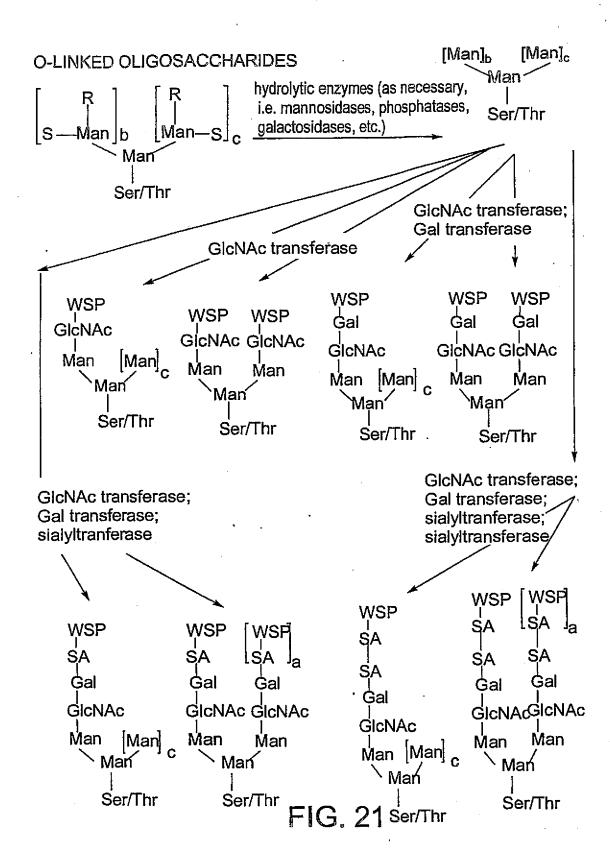
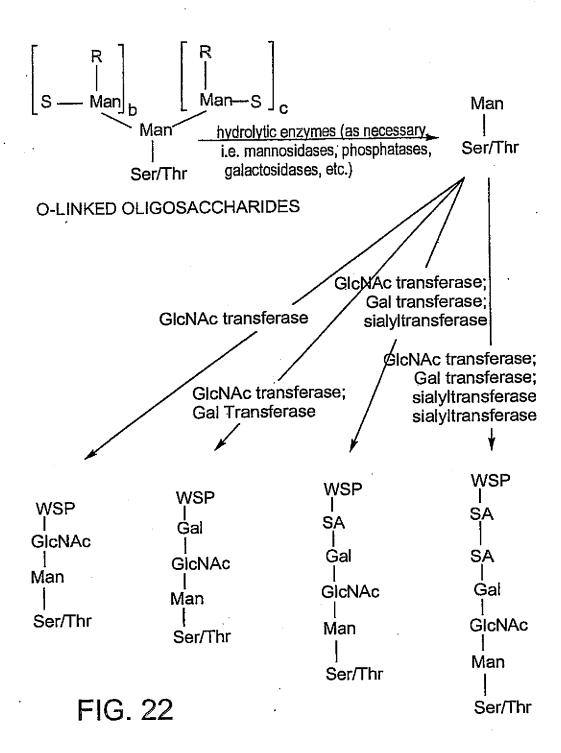
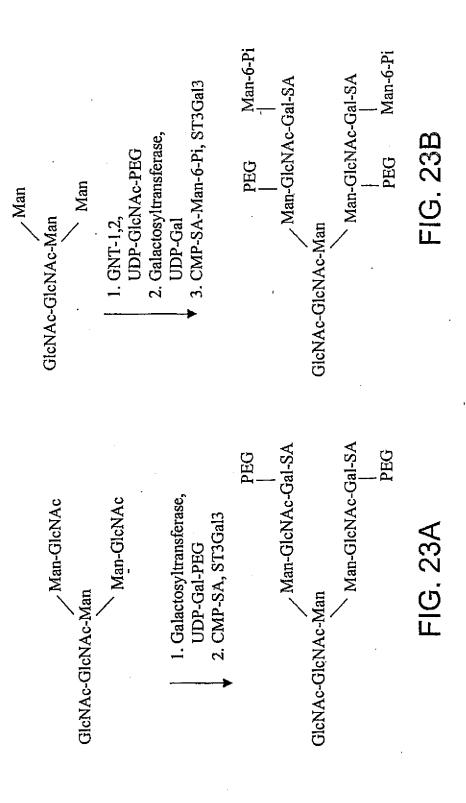
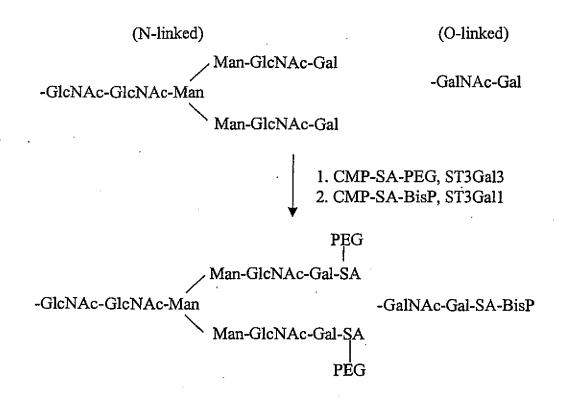


FIG. 20









BisP =Linker-HN-CH(PO₃)₂

FIG. 23C

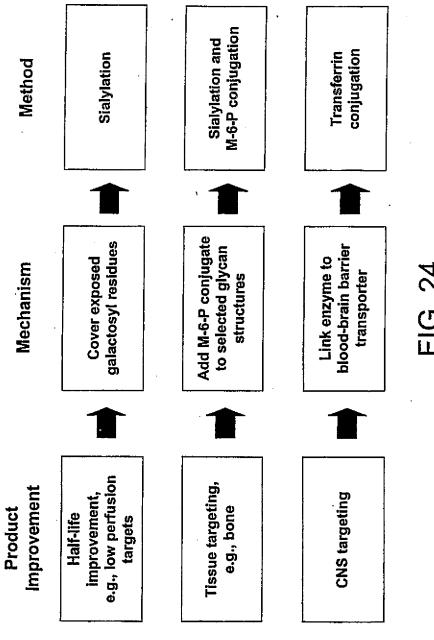
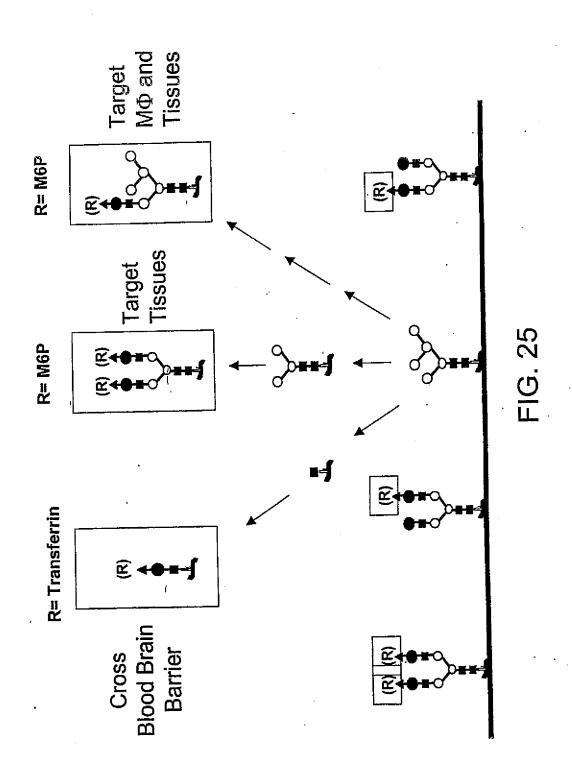
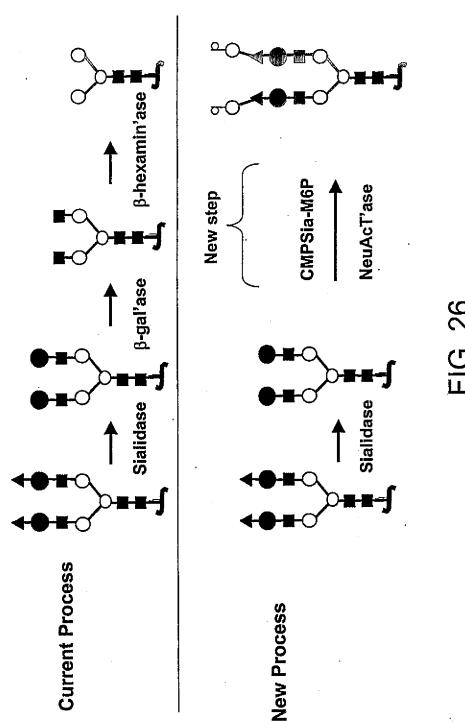
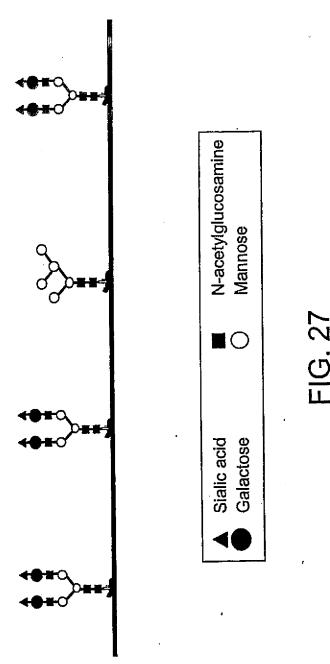


FIG. 24







Al-201 - Autolmmune 12AP1/E5 -- Viventia Biotech Al-301 – Autolmmune 1964 -- Aventis AIDS vaccine - ANRS, CIBG, Hesed 20K growth hormone -- AMUR Biomed, Hollis-Eden, Rome, United 28P6/E6 -- Viventia Biotech Biomedical, American Home Products, 3-Hydroxyphthaloyl-beta-lactoglobulin -Maxygen 4-IBB ligand gene therapy -64-Cu MAb conjugate TETA-1A3 -airway receptor ligand - IC Innovations Mallinckrodt Institute of Radiology AJvW 2 – Ajinomoto 64-Cu MAb conjugate TETA-cT84.66 AK 30 NGF -- Alkermes Albuferon -- Human Genome Sciences 64-Cu Trastuzumab TETA conjugate albumin - Biogen, DSM Anti-Infectives, Genentech Genzyme Transgenics, PPL Therapeutics, A 200 -- Amgen TranXenoGen, Welfide Corp. A10255 - Eli Liliy aldesleukin -- Chiron A1PDX - Hedral Therapeutics alefacept -- Biogen A6 -- Angstrom Alemtuzumab aaAT-III -- Genzyme Allergy therapy -- ALK-Abello/Maxygen, Abciximab - Centocor ALK-Abello/RP Scherer ABI.001 - Atlantic BioPharmaceuticals allergy vaccines -- Allergy Therapeutics ABT-828 - Abbott Alnidofibatide -- Aventis Pasteur Accutin Alnorine -- SRC VB VECTOR Actinohivin ALP 242 -- Gruenenthal activin - Biotech Australia, Human Alpha antitrypsin -- Arriva/Hyland Therapeutics, Curis Immuno/ProMetic/Protease Sciences AD 439 - Tanox Alpha-1 antitrypsin - Cutter, Bayer, PPL AD 519 - Tanox Therapeutics, Profile, ZymoGenetics, Adalimumab -- Cambridge Antibody Tech. Arriva Adenocarcinoma vaccine - Biomira - NIS Alpha-1 protease inhibitor -- Genzyme Adenosine deanimase -- Enzond Transgenics, Welfide Corp. Adenosine A2B receptor antagonists --Alpha-galactose fusion protein -Adenosine Therapeutics **Immunomedics** ADP-001 - Axis Genetics Alpha-galactosidase A -- Research AF 13948 – Affymax Corporation Technologies, Genzyme Afelimomab – Knoll Alpha-glucosidase - Genzyme, Novazyme AFP-SCAN - Immunomedics Alpha-lactalbumin AG 2195 - Corixa Alpha-L-iduronidase -- Transkaryotic agalsidase alfa -- Transkaryotic Therapies Therapies, BioMarin agalsidase beta -- Genzyme alteplase -- Genentech AGENT- Antisoma alvircept sudotox -- NIH Al 300 – Autolmmune ALX1-11 -sNPS Pharmaceuticals Al-101 - Teva Alzheimer's disease gene therapy Al-102 - Teva

FIG. 28A

| AM-133 AMRAD | Anti-angiogenesis monoclonal antibodies - |
|---|---|
| Amb a 1 immunostim conj. – Dynavax | KS Biomedix/Schering AG |
| AMD 3100 - AnorMED NIS | Anti-B4 MAb-DC1 conjugate ImmunoGen |
| AMD 3465 – AnorMED NIS | Anti-B7 antibody PRIMATIZED - IDEC |
| AMD 3465 – AnorMED NIS | Anti-B7-1 MAb 16-10A1 |
| AMD Fab Genentech | Anti-B7-1 MAb 1G10 |
| Amediplase – Menarini, Novartis | Anti-B7-2 MAb GL-1 |
| AM-F9 | Anti-B7-2-gelonin immunotoxin – |
| Amoebiasis vaccine | Antibacterials/antifungals |
| Amphiregulin Octagene | Diversa/IntraBiotics |
| anakinra – Amgen | Anti-beta-amyloid monoclonal antibodies |
| analgesic Nobex | Cambridge Antibody Tech., Wyeth-Ayerst |
| ancestim Amgen | Anti-BLyS antibodies Cambridge |
| AnergiX.RA – Corixa, Organon | Antibody Tech. /Human Genome Sciences |
| Angiocidin – InKine | Antibody-drug conjugates Seattle |
| angiogenesis inhibitors ILEX | Genetics/Eos |
| AngioMab – Antisoma | Anti-C5 MAb BB5-1 Alexion |
| Angiopoietins Regeneron/Procter & | Anti-C5 MAb N19-8 Alexion |
| Gamble | Anti-C8 MAb |
| angiostatin EntreMed | anticancer cytokines BioPulse |
| Angiostatin/endostatin gene therapy | anticancer matrix - Telios Integra |
| Genetix Pharmaceuticals | Anticancer monoclonal antibodies - ARIUS, |
| angiotensin-II, topical Maret | Immunex |
| Anthrax – EluSys Therapeutics/US Army | anticancer peptides Maxygen, Micrologix |
| Medical Research Institute | Anticancer prodrug Tech Alexion |
| Anthrax vaccine | Antibody Technologies |
| Anti platelet-derived growth factor D human | |
| monoclonal antibodies CuraGen | anticancer vaccine NIH |
| Anti-17-1A MAb 3622W94 | anticancers - Epimmune |
| GlaxoSmithKline | Anti-CCR5/CXCR4 sheep MAb KS |
| Anti-2C4 MAb Genentech | Biomedix Holdings |
| anti-4-1BB monoclonal antibodies Bristol | · Anti-CD11a MAb KBA |
| Myers Squibb | Anti-CD11a MAb M17 |
| Anti-Adhesion Platform Tech Cytovax | Anti-CD11a MAb TA-3 |
| Anti-adipocyte MAb Cambridge Antibody | Anti-CD11a MAb WT.1 |
| Tech./ObeSys | Anti-CD11b MAb Pharmacia |
| antiallergics Maxygen | Anti-CD11b MAb LM2 |
| antiallergy vaccine - Acambis | Anti-CD154 MAb Biogen |
| Anti-alpha-4-integrin MAb | Anti-CD16-anti-CD30 MAb Biotest |
| Anti-alphavβ3 integrin MAb – Applied | Anti-CD18 MAb — Pharmacia |
| Molecular Evolution | Anti-CD19 MAb B43 – |

FIG. 28B

| conjugate – Anti-CD147 Anti-CD19 MAb-saporin conjugate – Anti-CD19-dsFv-PE38-immunotoxin – | Anti-CD4 MAb 4162W94 — GlaxoSmithKline Anti-CD4 MAb B-F5 — Diaclone Anti-CD4 MAb GK1-5 Anti-CD4 MAb KT6 Anti-CD4 MAb OX38 |
|---|---|
| Anti-CD2 MAb 12-15 – | Anti-CD4 MAb PAP conjugate Bristol- |
| Anti-CD2 MAb B-E2 Diaclone | Myers Squibb |
| Anti-CD2 MAb OX34 – | Anti-CD4 MAb RIB 5-2 |
| Anti-CD2 MAb OX54 – Anti-CD2 MAb OX55 – | Anti-CD4 MAb W3/25 |
| Anti-CD2 MAb CA35 = Anti-CD2 MAb RM2-1 | Anti-CD4 MAb YTA 3.1.2 |
| Anti-CD2 MAb RM2-1 | Anti-CD4 MAb YTS 177-9 |
| Anti-CD2 MAD RM2-2 Anti-CD2 MAD RM2-4 | Anti-CD40 ligand MAb 5c8 Biogen Anti-CD40 MAb |
| Anti-CD20 MAb BCA B20 | Anti-CD40 MAb 5D12 – Tanox |
| Anti-CD20-anti-Fc alpha RI bispecific MAb - | |
| Medarex, Tenovus | Anti-CD44 MAb GKWA3 |
| Anti-CD22 MAb-saporin-6 complex – | Anti-CD44 MAb IM7 |
| Anti-CD3 immunotoxin – | Anti-CD44 MAb KM81 |
| Anti-CD3 MAb 145-2C11 Pharming | Anti-CD44 variant monoclonal antibodies |
| Anti-CD3 MAb CD4lgG conjugate | Corixa/Hebrew University |
| Genentech | Anti-CD45 MAb BC8-I-131 |
| Anti-CD3 MAb humanised - Protein Design | , Anti-CD45RB MAb |
| RW Johnson | Anti-CD48 MAb HuLy-m3 |
| Anti-CD3 MAb WT32 | Anti-CD48 MAb WM-63 |
| Anti-CD3 MAb-ricin-chain-A conjugate – | Anti-CD5 MAb Becton Dickinson |
| Anti-CD3 MAb-xanthine-oxidase conjugate | Anti-CD5 MAb OX19 |
| - | Anti-CD6 MAb |
| Anti-CD30 MAb BerH2 Medac | Anti-CD7 MAb-PAP conjugate |
| Anti-CD30 MAb-saporin conjugate | Anti-CD7 MAb-ricin-chain-A conjugate |
| Anti-CD30-scFv-ETA'-immunotoxin | Anti-CD8 MAb – Amerimmune, Cytodyn, |
| Anti-CD38 MAb AT13/5 | Becton Dickinson |
| Anti-CD38 MAb-saporin conjugate | Anti-CD8 MAb 2-43 |
| Anti-CD3-anti-CD19 bispecific MAb Anti-CD3-anti-EGFR MAb | Anti-CD8 MAb OX8 |
| | Anti-CD80 MAb P76C10 IDEC |
| Anti-CD3-anti-interleukin-2-receptor MAb Anti-CD3-anti-MOv18 MAb — Centocor | Anti-CD80 MAb P7C10 ID Vaccine Anti-CD8-idarubicin conjugate |
| Anti-CD3-anti-SCLC bispecific MAb | Anti-CEA MAb CE-25 |
| Anti-CD4 idiotype vaccine | Anti-CEA MAb MN 14 – Immunomedics |
| Anti-CD4 MAb – Centocor, IDEC | Anti-CEA MAb MN14-PE40 conjugate – |
| Pharmaceuticals, Xenova Group | Immunomedics |
| Anti-CD4 MAb 16H5 | • |
| | |

FIG. 28C

Anti-CEA MAb T84.66-interleukin-2 Anti-heparanase human monoclonal antibodies - Oxford conjugate Glycosciences/Medarex Anti-CEA sheep MAb -- KS Biomedix Anti-hepatitis C virus human monoclonal Holdings antibodies -- XTL Biopharmaceuticals Anti-cell surface monoclonal antibodies -Anti-HER-2 antibody gene therapy Cambridge Antibody Tech. /Pharmacia Anti-c-erbB2-anti-CD3 bifunctional MAb --Anti-herpes antibody - Epicyte Anti-HIV antibody -- Epicyte Otsuka anti-HIV catalytic antibody -- Hesed Biomed Anti-CMV MAb -- Scotgen anti-HIV fusion protein -- Idun Anti-complement anti-HIV proteins - Cangene Anti-CTLA-4 MAb Anti-HM1-24 MAb -- Chugai Anti-EGFR catalytic antibody -- Hesed Anti-hR3 MAb Anti-Human-Carcinoma-Antigen MAb -anti-EGFR immunotoxin -- IVAX **Epicyte** Anti-EGFR MAb -- Abgenix Anti-ICAM-1 MAb - Boehringer Ingelheim Anti-EGFR MAb 528 Anti-EGFR MAb KSB 107 -- KS Biomedix . Anti-ICAM-1 MAb 1A-29 -- Pharmacia Anti-ICAM-1 MAb HA58 Anti-EGFR MAb-DM1 conjugate --Anti-ICAM-1 MAb YN1/1.7.4 ImmunoGen Anti-ICAM-3 MAb ICM3 -- ICOS Anti-EGFR MAb-LA1 --Anti-idiotype breast cancer vaccine 11D10 Anti-EGFR sheep MAb -- KS Biomedix Anti-idiotype breast cancer vaccine Anti-FAP MAb F19-I-131 ACA14C5 --Anti-Fas IgM MAb CH11 Anti-idiotype cancer vaccine -- ImClone Anti-Fas MAb Jo2 Systems/Merck KGaA ImClone, Viventia Anti-Fas MAb RK-8 Anti-Flt-1 monoclonal antibodies -- ImClone Anti-idiotype cancer vaccine 1A7 -- Titan Anti-fungal peptides -- State University of Anti-idiotype cancer vaccine 3H1 -- Titan New York Anti-idiotype cancer vaccine TriAb -- Titan antifungal tripeptides - BTG Anti-ganglioside GD2 antibody-interleukin-2 Anti-idiotype Chlamydia trachomatis vaccine fusion protein -- Lexigen Anti-idiotype colorectal cancer vaccine --Anti-GM2 MAb -- Kyowa Novartis Anti-GM-CSF receptor monoclonal Anti-idiotype colorectal cancer vaccine antibodies -- AMRAD Anti-gp130 MAb -- Tosoh Anti-idiotype melanoma vaccine -- IDEC Anti-HCA monoclonal antibodies --Pharmaceuticals | AltaRex/Epigen Anti-idiotype ovarian cancer vaccine ACA Anti-hCG antibodies - Abgenix/AVI BioPharma Anti-idiotype ovarian cancer vaccine AR54 -- AltaRex

FIG. 28D

Anti-L-selectin monoclonal antibodies --Anti-idiotype ovarian cancer vaccine CA-Protein Design Labs, Abgenix, Stanford 125 – AltaRex, Biomira Anti-IgE catalytic antibody -- Hesed Biomed University Anti-MBL monoclonal antibodies --Anti-IgE MAb E26 -- Genentech Alexion/Brigham and Women's Hospital Anti-IGF-1 MAb Anti-MHC monoclonal antibodies anti-inflammatory -- GeneMax Anti-MIF antibody humanised – IDEC, anti-inflammatory peptide -- BTG Cytokine PharmaSciences anti-integrin peptides -- Burnha Anti-interferon-alpha-receptor MAb 64G12 - Anti-MRSAVRSA sheep MAb -- KS Pharma Pacific Management Biomedix Holdings Anti-interferon-gamma MAb -- Protein Anti-mu MAb -- Novartis Anti-MUC-1 MAb Design Labs Anti-interferon-gamma polyclonal antibody - Anti-MUC 18 Anti-Nogo-A MAb IN1 - Advanced Biotherapy Anti-nuclear autoantibodies -- Procyon Anti-interleukin-10 MAb -Anti-ovarian cancer monoclonal antibodies -Anti-interleukin-12 MAb --Anti-interleukin-1-beta polyclonal antibody -- - Dompe Anti-p185 monoclonal antibodies R&D Systems Anti-p43 MAb Anti-interleukin-2 receptor MAb 2A3 Anti-interleukin-2 receptor MAb 33B3-1 --Antiparasitic vaccines Anti-PDGF/bFGF sheep MAb -- KS Immunotech Biomedix Anti-interleukin-2 receptor MAb ART-18 Anti-properdin monoclonal antibodies --Anti-interleukin-2 receptor MAb LO-Tact-1 Abgenix/Gliatech Anti-interleukin-2 receptor MAb Mikbeta1 Anti-interleukin-2 receptor MAb NDS61 Anti-PSMA (prostrate specific membrane antigen) Anti-interleukin-4 MAb 11B11 Anti-interleukin-5 MAb - Wallace Anti-PSMA MAb J591 -- BZL Biologics Anti-Rev MAb gene therapy -Laboratories Anti-RSV antibodies - Epicyte, Intracell Anti-interleukin-6 MAb - Centocor, Anti-RSV monoclonal antibodies --Diaclone, Pharmadigm Medarex/Medimmune, Applied Molecular Anti-interleukin-8 MAb - Abgenix Anti-interleukin-8 MAb - Xenotech Evolution/Medimmune Anti-RSV MAb, inhalation --Anti-JL1 MAb Alkermes/Medimmune Anti-Klebsiella sheep MAb -- KS Biomedix Anti-RT gene therapy Antisense K-ras RNA gene therapy Anti-Laminin receptor MAb-liposomal doxorubicin conjugate Anti-SF-25 MAb Anti-sperm antibody -- Epicyte Anti-LCG MAb -- Cytoclonal Anti-lipopolysaccharide MAb -- VitaResc Anti-Tac(Fv)-PE38 conjugate Anti-TAPA/CD81 MAb AMP1 Anti-tat gene therapy

FIG. 28E

AOP-RANTES — Senetek Anti-TCR-alphabeta MAb H57-597 Apan-CH - Praecis Pharmaceuticals Anti-TCR-alphabeta MAb R73 APC-8024 - Demegen Anti-tenascin MAb BC-4-I-131 ApoA-1 - Milano, Pharmacia Anti-TGF-beta human monoclonal antibodies -- Cambridge Antibody Tech., Apogen -- Alexion apolipoprotein A1 - Avanir Genzyme Apolipoprotein E - Bio-Tech. General Anti-TGF-beta MAb 2G7 – Genentech Applaggin - Biogen Antithrombin III - Genzyme Transgenics, aprotinin - ProdiGene Aventis, Bayer, Behringwerke, CSL, APT-070C - AdProTech Myriad AR 177 - Aronex Pharmaceuticals Anti-Thy1 MAb AR 209 -- Aronex Pharmaceuticals, Anti-Thy1.1 MAb Anti-tissue factor/factor VIIA sheep MAb -**Antigenics** AR545C KS Biomedix ARGENT gene delivery systems - ARIAD Anti-TNF monoclonal antibodies -Centocor, Chiron, Peptech, Pharacia, Arresten ART-123 - Asahi Kasei Serono arvisulfatase B -- BioMarin Anti-TNF sheep MAb -- KS Biomedix Arvisulfatase B, Recombinant human --Holdings Anti-TNFalpha MAb -- Genzyme BioMarin Anti-TNFalpha MAb B-C7 -- Diacione AS 1051 — Ajinomoto ASI-BCL - Intracell Anti-tooth decay MAb -- Planet BioTech. Asparaginase - Merck Anti-TRAIL receptor-1 MAb -- Takeda ATL-101 - Alizyme Antitumour RNases - NIH Atrial natriuretic peptide - Pharis Anti-VCAM MAb 2A2 -- Alexion Aurintricarboxylic acid-high molecular Anti-VCAM MAb 3F4 -- Alexion weight Anti-VCAM-1 MAb Autoimmune disorders -- GPC Anti-VEC MAb - ImClone Biotech/MorphoSys Anti-VEGF MAb -- Genentech Autoimmune disorders and transplant Anti-VEGF MAb 2C3 rejection -- Bristol-Myers Squibb/Genzyme Anti-VEGF sheep MAb - KS Biomedix Holdings Autoimmune disorders/cancer --Anti-VLA-4 MAb HP1/2 -- Biogen Abgenix/Chiron, CuraGen Anti-VLA-4 MAb PS/2 Autotaxin Anti-VLA-4 MAb R1-2 Avicidin - NeoRx Anti-VLA-4 MAb TA-2 axogenesis factor-1 - Boston Life Sciences Anti-VAP-1 human MAb Axokine - Regeneron Anti-VRE sheep MAb -- KS Biomedix B cell lymphoma vaccine - Biomira Holdings B7-1 gene therapy -ANUP -- TranXenoGen BABS proteins - Chiron ANUP-1 -- Pharis

FIG. 28F

BMP 2 -- Genetics Institute/Medtronic-BAM-002 -- Novelos Therapeutics Basiliximab (anti CD25 MAb) - Novartis Sofamor Danek, Genetics Institute/ Collagenesis, Genetics Bay-16-9996 -- Bayer Institute/Yamanouch Bay-39-9437 -- Bayer BMP 2 gene therapy Bay-50-4798 -- Bayer BMP 52 -- Aventis Pasteur, Biopharm BB-10153 -- British Biotech BMP-2 - Genetics Institute BBT-001 - Bolder BioTech. BMS 182248 -- Bristol-Myers Squibb BBT-002 -- Bolder BioTech. BMS 202448 -- Bristol-Myers Squibb BBT-003 -- Bolder BioTech. bone growth factors - IsoTis BBT-004 -- Bolder BioTech. BPC-15 -- Pfizer BBT-005 -- Bolder BioTech. brain natriuretic peptide -BBT-006 -- Bolder BioTech. Breast cancer - Oxford BBT-007 -- Bolder BioTech. GlycoSciences/Medarex BCH-2763 -- Shire Breast cancer vaccine -- Therion Biologics, BCSF - Millenium Biologix Oregon BDNF - Regeneron - Amgen Becaplermin -- Johnson & Johnson, Chiron BSSL -- PPL Therapeutics BST-2001 - BioStratum Bectumomab - Immunomedics BST-3002 -- BioStratum Beriplast -- Aventis Beta-adrenergic receptor gene therapy -BTI 322 butyrylcholinesterase -- Shire University of Arkansas C 6822 -- COR Therapeutics bFGF -- Scios C1 esterase inhibitor -- Pharming BI 51013 -- Behringwerke AG C3d adjuvant -- AdProTech BIBH 1 - Boehringer Ingelheim CAB-2.1 -- Millennium BIM-23190 -- Beaufour-ipsen calcitonin - Inhale Therapeutics Systems, birch pollen immunotherapy - Pharmacia Aventis, Genetronics, TranXenoGen, bispecific fusion proteins - NIH Unigene, Rhone Poulenc Rohrer Bispecific MAb 2B1 -- Chiron calcitonin -- oral -- Nobex, Emisphere, Bitistatin Pharmaceutical Discovery BIWA 4 -- Boehringer Ingelheim Calcitonin gene-related peptide -- Asahi blood substitute - Northfield, Baxter Inti. Kasei -- Unigene BLP-25 -- Biomira BLS-0597 -- Boston Life Sciences calcitonin, human -- Suntory calcitonin, nasal -- Novartis, Unigene BLyS -- Human Genome Sciences calcitonin, Panoderm -- Elan BLyS radiolabelled - Human Genome calcitonin, Peptitrol - Shire Sciences calcitonin, salmon -- Therapicon BM 06021 -- Boehringer Mannheim calin -- Biopharm BM-202 -- BioMarin Calphobindin I BM-301 -- BioMarin calphobindin I -- Kowa BM-301 -- BioMarin calreticulin -- NYU BM-302 -- BioMarin

FIG. 28G

CD4 fusion toxin - Senetek Campath-1G CD4 IgG - Genentech Campath-1M CD4 receptor antagonists -cancer therapy -- Cangene cancer vaccine - Aixlie, Aventis Pasteur, Pharmacopeia/Progenics CD4 soluble -- Progenics Center of Molecular Immunology, YM CD4, soluble - Genzyme Transgenics BioSciences, Cytos, Genzyme, CD40 ligand - Immunex Transgenics, Globelmmune, Igeneon; CD4-ricin chain A - Genentech ImClone, Virogenetics, InterCell, Iomai, CD59 gene therapy -- Alexion Jenner Biotherapies, Memorial Sloan-Kettering Cancer Center, Sydney Kimmel CD8 TIL cell therapy -- Aventis Pasteur CD8, soluble -- Avidex Cancer Center, Novavax, Protein CD95 ligand - Roche Sciences, Argonex, SIGA CDP 571 - Celftech Cancer vaccine ALVAC-CEA B7.1 --CDP 850 - Celltech Aventis Pasteur/Therion Biologics CDP-860 (PEG-PDGF MAb) -- Celltech Cancer vaccine CEA-TRICOM -- Aventis CDP 870 -- Celltech Pasteur/Therion Biologics CDS-1 -- Emest Orlando Cancer vaccine gene therapy -- Cantab Cedelizumab -- Ortho-McNeil **Pharmaceuticals** Cetermin -- Insmed Cancer vaccine HER-2/neu -- Corixa CETP vaccine -- Avant Cancer vaccine THERATOPE -- Biomira Cetrorelix cancer vaccine, PolyMASC -- Valentis Cetuximab Candida vaccine -- Corixa, Inhibitex CGH 400 -- Novartis Canstatin - ILEX CGP 42934 - Novartis CAP-18 -- Panorama CGP 51901 - Tanox Cardiovascular gene therapy – Collateral CGRP - Unigene Therapeutics CGS 27913 -- Novartis carperitide - Suntory CGS 32359 - Novartis Casocidin-1 -- Pharis Chagas disease vaccine -- Corixa CAT 152 - Cambridge Antibody Tech. chemokines -- Immune Response CAT 192 -- Cambridge Antibody Tech. CAT 213 - Cambridge Antibody Tech. CHH 380 -- Novartis chitinase - Genzyme, ICOS Catalase— Enzon Chlamydia pneumoniae vaccine -- Antex Cat-PAD - Circassia **Biologics** CB 0006 - Celltech Chlamydia trachomatis vaccine -- Antex CCK(27-32)-- Akzo Nobel **Biologics** CCR2-641 -- NIH Chlamydia vaccine - GlaxoSmithKline CD, Procept -- Paligent Cholera vaccine CVD 103-HgR - Swiss CD154 gene therapy Serum and Vaccine Institute Berne CD39 -- Immunex Cholera vaccine CVD 112 -- Swiss Serum CD39-L2 -- Hyseq and Vaccine Institute Berne CD39-L4 -- Hyseq

FIG. 28H

| Cholera vaccine inactivated oral – SBL | CRL 1605 CytRx |
|---|--|
| Vaccin | CS-560 - Sankyo |
| Chrysalin Chrysalis BioTech. | CSF ZymoGenetics |
| CI-782 – Hitachi Kase | CSF-G - Hangzhou, Dong-A, Hanmi |
| Ciliary neurotrophic factor - Fidia, Roche | CSF-GM - Cangene, Hunan, LG Chem |
| CIM project Active Biotech | CSF-M - Zarix |
| CL 329753 - Wyeth-Ayerst | CT 1579 - Merck Frosst |
| CL22, Cobra ML Laboratories | CT 1786 – Merck Frosst |
| Clenoliximab IDEC | CT-112 [^] BTG |
| Clostridium difficile antibodies Epicyte | CTB-134L Xenova |
| clotting factors Octagene | CTC-111 Kaketsuken |
| CMB 401 Celltech | CTGF FibroGen |
| CNTF Sigma-Tau | CTLA4-lg Bristol-Myers Squibb |
| Cocaine abuse vaccine - Cantab, | CTLA4-lg gene therapy |
| ImmuLogic, Scripps | CTP-37 – AVI BioPharma |
| coccidiomycosis vaccine Arizo | C-type natriuretic peptide – Suntory |
| collagen - Type I - Pharming | CVS 995 – Corvas Intl. |
| Collagen formation inhibitors - FibroGen | CX 397 – Nikko Kyodo |
| Collagen/hydroxyapatite/bone growth factor | CY 1747 – Epimmune |
| Aventis Pasteur, Biopharm, Orquest | CY 1748 Epimmune |
| collagenase BioSpecifics | Cyanovirin-N |
| Colorectal cancer vaccine Wistar Institute | Cystic fibrosis therapy CBR/IVAX |
| Component B, Recombinant Serono | CYT 351 |
| Connective tissue growth factor inhibitors | tilli Tillia i Danasasa |
| COURTECTIAE figgine Atomitt ractor immercia | cytokine Traps Regeneron |
| FibroGen/Taisho | cytokines – Enzon, Cytoclonal |
| | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – |
| FibroGen/Taisho | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – Chiron, Aquila Biopharmaceuticals, |
| FibroGen/Taisho Contortrostatin contraceptive vaccine Zonagen Contraceptive vaccine hCG | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – Chiron, Aquila Biopharmaceuticals, Aventis Pasteur, Virogenetics |
| FibroGen/Taisho Contortrostatin contraceptive vaccine Zonagen | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – Chiron, Aquila Biopharmaceuticals, Aventis Pasteur, Virogenetics Cytomegalovirus vaccine live – Aventis |
| FibroGen/Taisho Contortrostatin contraceptive vaccine Zonagen Contraceptive vaccine hCG Contraceptive vaccine male reversible IMMUCON | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – Chiron, Aquila Biopharmaceuticals, Aventis Pasteur, Virogenetics Cytomegalovirus vaccine live – Aventis Pasteur |
| FibroGen/Taisho Contortrostatin contraceptive vaccine Zonagen Contraceptive vaccine hCG Contraceptive vaccine male reversible IMMUCON Contraceptive vaccine zona pellucida | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – Chiron, Aquila Biopharmaceuticals, Aventis Pasteur, Virogenetics Cytomegalovirus vaccine live – Aventis |
| FibroGen/Taisho Contortrostatin contraceptive vaccine Zonagen Contraceptive vaccine hCG Contraceptive vaccine male reversible IMMUCON Contraceptive vaccine zona pellucida Zonagen | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – Chiron, Aquila Biopharmaceuticals, Aventis Pasteur, Virogenetics Cytomegalovirus vaccine live – Aventis Pasteur Cytosine deaminase gene therapy – GlaxoSmithKline |
| FibroGen/Taisho Contortrostatin contraceptive vaccine Zonagen Contraceptive vaccine hCG Contraceptive vaccine male reversible IMMUCON Contraceptive vaccine zona pellucida Zonagen Copper-64 labelled MAb TETA-1A3 NCI | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – Chiron, Aquila Biopharmaceuticals, Aventis Pasteur, Virogenetics Cytomegalovirus vaccine live – Aventis Pasteur Cytosine deaminase gene therapy – |
| FibroGen/Taisho Contortrostatin contraceptive vaccine Zonagen Contraceptive vaccine hCG Contraceptive vaccine male reversible iMMUCON Contraceptive vaccine zona pellucida Zonagen Copper-64 labelled MAb TETA-1A3 NCI Coralyne | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – Chiron, Aquila Biopharmaceuticals, Aventis Pasteur, Virogenetics Cytomegalovirus vaccine live – Aventis Pasteur Cytosine deaminase gene therapy – GlaxoSmithKline DA-3003 – Dong-A |
| FibroGen/Taisho Contortrostatin contraceptive vaccine Zonagen Contraceptive vaccine hCG Contraceptive vaccine male reversible IMMUCON Contraceptive vaccine zona pellucida Zonagen Copper-64 labelled MAb TETA-1A3 NCI Coralyne Corsevin M | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – Chiron, Aquila Biopharmaceuticals, Aventis Pasteur, Virogenetics Cytomegalovirus vaccine live – Aventis Pasteur Cytosine deaminase gene therapy – GlaxoSmithKline DA-3003 – Dong-A DAB389interleukin-6 – Senetek |
| FibroGen/Taisho Contortrostatin contraceptive vaccine Zonagen Contraceptive vaccine hCG Contraceptive vaccine male reversible iMMUCON Contraceptive vaccine zona pellucida Zonagen Copper-64 labelled MAb TETA-1A3 NCI Coralyne | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – Chiron, Aquila Biopharmaceuticals, Aventis Pasteur, Virogenetics Cytomegalovirus vaccine live – Aventis Pasteur Cytosine deaminase gene therapy – GlaxoSmithKline DA-3003 – Dong-A DAB389interleukin-6 – Senetek DAB389interleukin-7 |
| FibroGen/Taisho Contortrostatin contraceptive vaccine Zonagen Contraceptive vaccine hCG Contraceptive vaccine male reversible IMMUCON Contraceptive vaccine zona pellucida Zonagen Copper-64 labelled MAb TETA-1A3 NCI Coralyne Corsevin M C-peptide analogues Schwarz CPI-1500 Consensus | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – Chiron, Aquila Biopharmaceuticals, Aventis Pasteur, Virogenetics Cytomegalovirus vaccine live – Aventis Pasteur Cytosine deaminase gene therapy – GlaxoSmithKline DA-3003 – Dong-A DAB389interleukin-6 – Senetek DAB389interleukin-7 Daclizumab (anti-IL2R MAb) – Protein |
| FibroGen/Taisho Contortrostatin contraceptive vaccine Zonagen Contraceptive vaccine hCG Contraceptive vaccine male reversible IMMUCON Contraceptive vaccine zona pellucida Zonagen Copper-64 labelled MAb TETA-1A3 NCI Coralyne Corsevin M C-peptide analogues Schwarz CPI-1500 Consensus CRF Neurobiological Tech. | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – Chiron, Aquila Biopharmaceuticals, Aventis Pasteur, Virogenetics Cytomegalovirus vaccine live – Aventis Pasteur Cytosine deaminase gene therapy – GlaxoSmithKline DA-3003 – Dong-A DAB389interleukin-6 – Senetek DAB389interleukin-7 Daclizumab (anti-IL2R MAb) – Protein Design Labs |
| FibroGen/Taisho Contortrostatin contraceptive vaccine Zonagen Contraceptive vaccine hCG Contraceptive vaccine male reversible iMMUCON Contraceptive vaccine zona pellucida Zonagen Copper-64 labelled MAb TETA-1A3 NCI Coralyne Corsevin M C-peptide analogues Schwarz CPI-1500 Consensus CRF Neurobiological Tech. cRGDfV pentapeptide | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – Chiron, Aquila Biopharmaceuticals, Aventis Pasteur, Virogenetics Cytomegalovirus vaccine live – Aventis Pasteur Cytosine deaminase gene therapy – GlaxoSmithKline DA-3003 – Dong-A DAB389interleukin-6 – Senetek DAB389interleukin-7 Daclizumab (anti-IL2R MAb) – Protein Design Labs DAMP^ – Incyte Genomics |
| FibroGen/Taisho Contortrostatin contraceptive vaccine Zonagen Contraceptive vaccine hCG Contraceptive vaccine male reversible IMMUCON Contraceptive vaccine zona pellucida Zonagen Copper-64 labelled MAb TETA-1A3 NCI Coralyne Corsevin M C-peptide analogues Schwarz CPI-1500 Consensus CRF Neurobiological Tech. | cytokines – Enzon, Cytoclonal Cytomegalovirus glycoprotein vaccine – Chiron, Aquila Biopharmaceuticals, Aventis Pasteur, Virogenetics Cytomegalovirus vaccine live – Aventis Pasteur Cytosine deaminase gene therapy – GlaxoSmithKline DA-3003 – Dong-A DAB389interleukin-6 – Senetek DAB389interleukin-7 Daclizumab (anti-IL2R MAb) – Protein Design Labs DAMP^ – Incyte Genomics Daniplestim – Pharmacia |

FIG. 281

Duteplase -- Baxter Intl. DCC -- Genzyme DWP-401 -- Daewoong DDF -- Hyseq DWP-404 -- Daewoong decorin ~ Integra, Telios defensins -- Large Scale Biology DWP-408 -- Daewoong Dx 88 (Epi-KAL2) -- Dyax DEGR-VIIa Dx 890 (elastin inhibitors) -- Dyax Delmmunised antibody 3B6/22 AGEN E coli O157 vaccine -- NIH Deimmunised anti-cancer antibodies --E21-R -- BresaGen Biovation/Viragen Eastern equine encephalitis virus vaccine -Dendroamide A Dengue vaccine -- Bavarian Nordic, Merck Echicetin --Echinhibin 1 denileukin diftitox -- Ligand Echistatin – Merck DES-1101 -- Desmos Echitamine desirudin -- Novartis Ecromeximab – Kyowa Hakko desmopressin -- Unigene Desmoteplase - Merck, Schering AG EC-SOD -- PPL Therapeutics Eculizumab (5G1.1) -- Alexion Destabilase Diabetes gene therapy - DeveloGen, Pfizer EDF -- Ajinomoto EDN derivative - NIH Diabetes therapy -- Crucell Diabetes type 1 vaccine - Diamyd EDNA -- NIH Edobacomab -- XOMA **Therapeutics** Edrecolomab -- Centocor DiaCIM -- YM BioSciences EF 5077 dialytic oligopeptides - Research Corp Efalizumab -- Genentech Diamyd -- Diamyd Therapeutics EGF fusion toxin - Seragen, Ligand DiaPep227-- Pepgen EGF-P64k vaccine -- Center of Molecular DiavaX -- Corixa Immunology Digoxin MAb -- Glaxo EL 246 - LigoCyte Diphtheria tetanus pertussis-hepatitis B elastase inhibitor - Synergen vaccine -- GlaxoSmithKline elcatonin - Therapicon DIR therapy - Solis Therapeutics -EMD 72000 -- Merck KGaA DNase - Genentech Emdogain -- BIORA Dornase alfa -- Genentech emfilermin -- AMRAD Dornase alfa, inhalation -- Genentech Emoctakin - Novartis Doxorubicin-anti-CEA MAb conjugate enamel matrix protein -- BIORA **Immunomedics** Endo III -- NYU DP-107 -- Trimeris endostatin -- EntreMed, Pharis drotrecogin alfa -- Eli Lilly Enhancins -- Micrologix DTctGMCSF Enlimomab - Isis Pharm. DTP-polio vaccine - Aventis Pasteur Enoxaparin sodium -- Pharmuka DU 257-KM231 antibody conjugate -enzyme linked antibody nutrient depletion Kvowa therapy -- KS Biomedix Holdings

FIG. 28J

dural graft matrix -- Integra

Factor VII -- Novo Nordisk, Bayer, Baxter Eosinophil-derived neutralizing agent -EP-51216 -- Asta Medica Intl. Factor VIIa - PPL Therapeutics, EP-51389 -- Asta Medica EPH family ligands - Regeneron ZvmoGenetics Epidermal growth factor - Hitachi Kasei, Factor VIII - Bayer Genentech, Beaufour-Ipsen, CLB, Inex, Octagen, Pharmacia, Johnson & Johnson Epidermal growth factor fusion toxin — Pharming Factor VIII -- PEGylated -- Bayer Senetek Factor VIII fragments -- Pharmacia Epidermal growth factor-genistein – Factor VIII gene therapy -- Targeted EPI-HNE-4 -- Dyax Genetics EPI-KAL2 -- Dyax Factor VIII sucrose formulation - Bayer, Epoetin-alfa -- Amgen, Dragon Pharmaceuticals, Nanjing Huaxin Genentech Factor VIII-2 -- Bayer Epratuzumab -- Immunomedics Factor VIII-3 -- Bayer Epstein-Barr virus vaccine --Factor Xa inhibitors - Merck, Novo Nordisk, Aviron/SmithKline Beecham, Bioresearch Mochida Eptacog alfa -- Novo Nordisk Factor XIII -- ZymoGenetics Eptifibatide -- COR Therapeutics Factors VIII and IX gene therapy -- Genetics erb-38 --Institute/Targeted Genetics Erlizumab -- Genentech erythropoietin -- Alkermes, ProLease, Dong-Famoxin -- Genset Fas (delta) TM protein - LXR BioTech. A, Elanex, Genetics Institute, LG Chem, Fas TR -- Human Genome Sciences Protein Sciences, Serono, Snow Brand, SRC VB VECTOR, Transkaryotic Felvizumab -- Scotgen FFR-VIIa - Novo Nordisk Therapies FG-001 -- F-Gene Erythropoietin Beta -- Hoffman La Roche FG-002 - F-Gene Erythropoietin/Epoetin alfa -- Chugai FG-004 - F-Gene Escherichia coli vaccine -- North American FG-005 - F-Gene Vaccine, SBL Vaccin, Swiss Serum and FGF + fibrin -- Repair Vaccine Institute Berne Fibrimage -- Bio-Tech. General etanercept -- Immunex fibrin-binding peptides — ISIS Innovation examorelin – Mediolanum fibringen – PPL Therapeutics, Pharming Exendin 4 -- Amylin fibroblast growth factor - Chiron, NYU, exonuclease VII Ramot, ZymoGenetics F 105 -- Centocor fibrolase conjugate - Schering AG F-992 -- Fornix Filgrastim -- Amgen Factor IX -- Alpha Therapeutics, Welfide filgrastim - PDA modified -- Xencor Corp., CSL, enetics Institute/AHP, FLT-3 ligand -- Immunex Pharmacia, PPL Therapeutics FN18 CRM9 -Factor IX gene therapy -- Cell Genesys

FIG. 28K

glutamate decarboxylase -- Genzyme follistatin -- Biotech Australia, Human Transgenics Therapeutics Glycoprotein S3 -- Kureha follitropin alfa - Alkermes, ProLease, PowderJect, Serono, Akzo Nobel GM-CSF -- Immunex GM-CSF tumour vaccine - PowderJect Follitropin Beta - Bayer, Organon GnRH immunotherapeutic -- Protherics FP 59 Goserelin (LhRH antagonist) -- AstraZeneca FSH -- Ferring gp75 antigen -- ImClone FSH + LH -- Ferring gp96 - Antigenics F-spondin -- CeNeS GPI 0100 - Galenica fusion protein delivery system -- UAB GR 4991W93 - GlaxoSmithKline Research Foundation Granulocyte colony-stimulating factor -fusion toxins -- Boston Life Sciences Dona-A G 5598 -- Genentech Granulocyte colony-stimulating factor GA-II -- Transkaryotic Therapies Gamma-interferon analogues -- SRC VB conjugate grass allergy therapy -- Dynavax VECTOR GRF1-44 -- ICN Ganirelix -- Roche Growth Factor - Chiron, Atrigel, Atrix, gastric lipase -- Meristem Innogenetics, ZymoGenetics, Novo Gavilimomab growth factor peptides -- Biotherapeutics G-CSF – Amgen, SRC VB VECTOR arowth hormone -- LG Chem GDF-1 -- CeNeS growth hormone, Recombinant human --GDF-5 -- Biopharm Serono GDNF (glial derived neurotrophic factor) --GT 4086 -- Gliatech Amgen GW 353430 -- GlaxoSmithKline gelsolin - Biogen GW-278884 -- GlaxoSmithKline Gemtuzumab ozogamicin -- Celltech H 11 - Viventia Biotech Gene-activated epoetin-alfa -- Aventis H5N1 influenza A virus vaccine -- Protein Pharma - Transkaryotic Therapies Sciences Glanzmann thrombasthenia gene therapy haemoglobin -- Biopure Glatiramer acetate -- Yeda haemoglobin 3011, Recombinant -- Baxter glial growth factor 2 - CeNeS Healthcare GLP-1 - Amylin, Suntory, TheraTech, haemoglobin crosfumaril - Baxter Intl. Watson haemoglobin stabilized -- Ajinomoto GLP-1 peptide analogues -- Zealand haemoglobin, recombinant -- Apex **Pharaceuticals** HAF - Immune Response glucagon -- Eli Lilly, ZymoGenetics Glucagon-like peptide-1 7-36 amide --Hantavirus vaccine HB 19 Suntory Glucogen-like peptide -- Amylin HBNF -- Regeneron HCC-1 — Pharis Glucocerebrosidase -- Genzyme hCG -- Milkhaus

FIG. 28L

Herpes simplex glycoprotein DNA vaccine – hCG vaccine - Zonagen Merck, Wyeth-Lederle Vaccines-Malvern, HE-317 -- Hollis-Eden Pharmaceuticals Genentech, GlaxoSmithKline, Chiron, Heat shock protein cancer and influenza Takeda vaccines -- StressGen Helicobacter pylori vaccine -- Acambis, Herpes simplex vaccine -- Cantab AstraZeneca/CSL, Chiron, Provalis Pharmaceuticals, CEL-SCI, Henderson Helistat-G -- GalaGen Morley Herpes simplex vaccine live -- ImClone Hemolink – Hemosol Systems/Wyeth-Lederle, Aventis Pasteur hepapoietin -- Snow Brand HGF derivatives -- Dompe heparanase - InSight hIAPP vaccine -- Crucell heparinase I -- Ibex Hib-hepatitis B vaccine -- Aventis Pasteur heparinase III -- Ibex Hepatitis A vaccine -- American Biogenetic HIC 1 HIP-- Altachem Sciences Hirudins - Biopharma, Cangene, Dongkook, Hepatitis A vaccine inactivated Japan Energy Corporation, Pharmacia Hepatitis A vaccine Nothav -- Chiron Corporation, SIR International, Sanofi-Hepatitis A-hepatitis B vaccine -Synthelabo, Sotragene, Rhein Biotech GlaxoSmithKline HIV edible vaccine -- ProdiGene hepatitis B therapy -- Tripep HIV gp120 vaccine - Chiron, Ajinomoto, Hepatitis B vaccine - Amgen, Chiron SpA, GlaxoSmithKline, ID Vaccine, Progenics, Meiji Milk, NIS, Prodeva, PowderJect, VaxGen Rhein Biotech HIV gp120 vaccine gene therapy -Hepatitis B vaccine recombinant -- Evans Vaccines, Epitec Combiotech, Genentech, HIV gp160 DNA vaccine - PowderJect, Aventis Pasteur, Oncogen, Hyland Medlmmune, Merck Sharp & Dohme, Immuno, Protein Sciences Rhein Biotech, Shantha Biotechnics, HIV gp41 vaccine -- Panacos Vector, Yeda Hepatitis B vaccine recombinant TGP 943 -- HIV HGP-30W vaccine -- CEL-SCI HIV immune globulin - Abbott, Chiron Takeda HIV peptides -- American Home Products Hepatitis C vaccine -- Bavarian Nordic, HIV vaccine -- Applied bioTech., Axis Chiron, Innogenetics Acambis, Genetics, Biogen, Bristol-Myers Squibb, Hepatitis D vaccine -- Chiron Vaccines Genentech, Korea Green Cross, NIS, Hepatitis E vaccine recombinant -Oncogen, Protein Sciences Corporation, Genelabs/GlaxoSmithKline, Novavax Terumo, Tonen Corporation, Wyethhepatocyte growth factor - Panorama, Ayerst, Wyeth-Lederle Vaccines-Malvern, Sosei Advanced BioScience Laboratories, hepatocyte growth factor kringle fragments -Bavarian Nordic, Bavarian Nordic/Statens EntreMed Serum Institute, GeneCure, Immune Her-2/Neu peptides -- Corixa Response, Progenics, Therion Biologics,

FIG. 28M

United Biomedical, Chiron

Human monoclonal antibodies --HIV vaccine vCP1433 - Aventis Pasteur HIV vaccine vCP1452 -- Aventis Pasteur Medarex/Northwest Biotherapeutics, Medarex/Seattle Genetics HIV vaccine vCP205 -- Aventis Pasteur human netrin-1 -- Exelixis HL-9 -- American BioScience human papillomavirus antibodies -- Epicyte HM-9239 -- Cytran Human papillomavirus vaccine -- Biotech HML-103 -- Hemosol Australia, IDEC, StressGen HML-104 -- Hemosol Human papillomavirus vaccine MEDI 501 --HML-105 -- Hemosol MedImmune/GlaxoSmithKline HML-109 -- Hemosol Human papillomavirus vaccine MEDI HML-110 -- Hemosol 503/MEDI 504 --HML-121 -- Hemosol MedImmune/GlaxoSmithKline hNLP -- Pharis Human papillomavirus vaccine TA-CIN --Hookworm vaccine Cantab Pharmaceuticals host-vector vaccines -- Henogen Human papillomavirus vaccine TA-HPV --HPM 1 -- Chugai Cantab Pharmaceuticals HPV vaccine -- MediGene Human papillomavirus vaccine TH-GW ---HSA -- Meristem Cantab/GlaxoSmithKline HSF -- StressGen human polyclonal antibodies - Biosite/Eos HSP carriers -- Weizmann, Yeda, Peptor BioTech./ Medarex HSPPC-70 -- Antigenics HSPPC-96, pathogen-derived -- Antigenics human type II anti factor VIII monoclonal antibodies -- ThromboGenics HSV 863 -- Novartis humanised anti glycoprotein lb murine HTLV-I DNA vaccine monoclonal antibodies -- ThromboGenics HTLV-I vaccine HumaRAD -- Intracell HTLV-II vaccine -- Access HuMax EGFR -- Genmab HU 901 - Tanox HuMax-CD4 - Medarex Hu23F2G -- ICOS HuMax-IL15 -- Genmab HuHMFG1 HYB 190 -- Hybridon HumaLYM -- Intracell HYB 676 -- Hybridon Human krebs statika -- Yamanouchi I-125 MAb A33 -- Celltech human monoclonal antibodies --Ibritumomab tiuxetan -- IDEC Abgenix/Biogen, Abgenix/ Corixa, Abgenix/Immunex, Abgenix/Lexicon, IBT-9401 -- Ibex IBT-9402 -- Ibex Abgenix/ Pfizer, Athersys/Medarex, IC 14 -- ICOS Biogen/MorphoSys, CAT/Searle, Idarubicin anti-Ly-2.1 --Centocor/Medarex, Corixa/Kirin Brewery, IDEC 114 -- IDEC Corixa/Medarex, Eos BioTech./Medarex, IDEC 131 - IDEC Eos/Xenerex, Exelixis/Protein Design IDEC 152 -- IDEC Labs, ImmunoGen/ Raven, Medarex/ B.Twelve, MorphoSys/ImmunoGen, XTL IDM 1 - IDM IDPS -- Hollis-Eden Pharmaceuticals Biopharmaceuticals/Dyax,

FIG. 28N

iduronate-2-sulfatase -- Transkaryotic insulin -- Autolmmune, Altea, Biobras, BioSante, Bio-Tech. General, Chong Kun Therapies Dang, Emisphere, Flamel, Provalis, Rhein IGF/IBP-2-13 -- Pharis IGN-101 -- Igeneon Biotech, TranXenoGen IK HIR02 -- Iketon insulin (bovine) -- Novartis insulin analogue -- Eli Lilly IL-11 — Genetics Institute/AHP Insulin Aspart -- Novo Nordisk IL-13-PE38 -- NeoPharm insulin detemir -- Novo Nordisk IL-17 receptor -- Immunex IL-18BP - Yeda insulin glargine -- Aventis insulin inhaled - Inhale Therapeutics IL-1Hy1 -- Hyseq Systems, Alkermes IL-1ß -- Celltech insulin oral -- Inovax IL-1ß adjuvant -- Celltech IL-2 -- Chiron insulin, AeroDose -- AeroGen IL-2 + IL-12 -- Hoffman La-Roche insulin, AERx -- Aradigm insulin, BEODAS -- Elan IL-6/sIL-6R fusion -- Hadasit insulin, Biphasix -- Helix IL-6R derivative -- Tosoh IL-7-Dap 389 fusion toxin -- Ligand insulin, buccal -- Generex insulin, I2R -- Flemington IM-862 -- Cytran insulin, intranasal -- Bentley IMC-1C11 -- ImClone insulin, oral -- Nobex, Unigene imiglucerase -- Genzyme insulin, Orasome -- Endorex Immune globulin intravenous (human) -insulin, ProMaxx -- Epic Hoffman La Roche insulin, Quadrant -- Elan immune privilege factor -- Proneuron insulin, recombinant -- Aventis Immunocal -- Immunotec insulin, Spiros -- Elan Immunogene therapy -- Briana Bio-Tech Immunoliposomal 5-fluorodeoxyuridineinsulin, Transfersome -- IDEA insulin, Zymo, recombinant -- Novo Nordisk dipalmitate -immunosuppressant vaccine -- Aixlie insulinotropin -- Scios Insulysin gene therapy immunotoxin -- Antisoma, NIH integrin antagonists -- Merck ImmuRAIT-Re-188 – Immunomedics interferon (Alpha2) -- SRC VB VECTOR, imreg-1 -- Imreg Viragen, Dong-A, Hoffman La-Roche, infertility -- Johnson & Johnson, E-TRANS Genentech Infliximab -- Centocor Influenza virus vaccine -- Aventis Pasteur, interferon - BioMedicines, Human Genome Protein Sciences Sciences inhibin - Biotech Australia, Human interferon (Alfa-n3)—Interferon Sciences Therapeutics interferon (Alpha), Biphasix -- Helix Inhibitory G protein gene therapy INKP-2001 -- InKine Inolimomab -- Diaclone

FIG. 280

interferon (Alpha)—Amgen, BioNative, IL-2/ diphtheria toxin - Ligand Interleukin-3 - Cangene Novartis, Genzyme Transgenics, Interleukin-4 - Immunology Ventures, Hayashibara, Inhale Therapeutics Sanofi Winthrop, Schering-Plough, Systems, Medusa, Flamel, Dong-A, Immunex/ Sanofi Winthrop, Bayer, Ono GeneTrol, Nastech, Shantha, interleukin-4 + TNF-Alpha -- NIH Wassermann, LG Chem, Sumitomo, interleukin-4 agonist -- Bayer Aventis, Behring EGIS, Pepgen, Servier, interleukin-4 fusion toxin - Ligand Rhein Biotech. Interleukin-4 receptor - Immunex, Immun interferon (Alpha2A) Interleukin-6 - Ajinomoto, Cangene, Yeda, interferon (Alpha2B) - Enzon, Schering-Genetics Institute, Novartis Plough, Biogen, IDEA interferon (Alpha-N1) -- GlaxoSmithKline interleukin-6 fusion protein interleukin-6 fusion toxin - Ligand, Serono interferon (beta) - Rentschier, GeneTrol, interleukin-7 -- IC Innovations Meristem, Rhein Biotech, Toray, Yeda, interleukin-7 receptor -- Immunex Daiichi, Mochida interleukin-8 antagonists -- Kyowa interferon (Beta1A) - Serono, Biogen Hakko/Millennium/Pfizer interferon (beta1A),inhale -- Biogen interleukin-9 antagonists -- Genaera interferon (ß1b)-- Chiron interleukin-10 - DNAX, Schering-Plough interferon (tau) - Pepgen: Interleukin-10 gene therapy -Interferon alfacon-1 - Amgen interleukin-12 -- Genetics Institute, Hoffman Interferon alpha-2a vaccine La-Roche Interferon Beta 1b - Schering/Chiron, interleukin-13 -- Sanofi interMune interleukin-13 antagonists - AMRAD Interferon Gamma -- Boehringer Ingelheim, interleukin-13-PE38QQR Sheffield, Rentschler, Hayashibara interleukin-15 -- Immunex interferon receptor, Type I - Serono interferon(Gamma1B) -- Genentech interleukin-16 - Research Corp interleukin-18 - GlaxoSmithKline Interferon-alpha-2b + ribavirin - Biogen, Interleukin-18 binding protein -- Serono ICN lor-P3 -- Center of Molecular Immunology interferon-alpha-2b gene therapy --IP-10 -- NIH Schering-Plough **IPF** -- Metabolex Interferon-con1 gene therapy -IR-501 -- Immune Response interleukin-1 antagonists -- Dompe ISIS 9125 - Isis Pharmaceuticals interleukin-1 receptor antagonist – Abbott ISURF No. 1554 -- Millennium Bioresearch, Pharmacia ISURF No. 1866 - Iowa State Univer. Interleukin-1 receptor type I — Immunex ITF-1697 -- Italfarmaco interleukin-1 receptor Type II -- Immunex IxC 162 -- Ixion Interleukin-1 trap -- Regeneron Interleukin-1-alpha -- Immunex/Roche J 695 -- Cambridge Antibody Tech., Genetics Inst., Knoli interleukin-2 - SRC VB VECTOR, Jagged + FGF -- Repair Ajinomoto, Biomira, Chiron

FIG. 28P

JKC-362 — Phoenix Pharmaceuticals leptin, 2nd-generation - Amgen leridistim - Pharmacia JTP-2942 – Japan Tobacce Juman monoclonal antibodies -leuprolide, ProMaxx -- Epic leuprorelin, oral -- Unigene Medarex/Raven LeuTech -- Papatin K02 -- Axys Pharmaceuticals LEX 032 -- SuperGen Keliximab - IDEC LiDEPT -- Novartis Keyhole limpet haemocyanin Lintuzumab (anti-CD33 MAb) -- Protein KGF -- Amgen KM 871 -- Kyowa Design Labs lipase -- Altus Biologics KPI 135 -- Scios lipid A vaccine -- EntreMed KPI-022 -- Scios lipid-linked anchor Tech. - ICRT, ID Kringle 5 **Biomedical** KSB 304 KSB-201 -- KS Biomedix liposome-CD4 Tech. -- Sheffield Listeria monocytogenes vaccine L 696418 -- Merck . LMB 1 L 703801 -- Merck LMB 7 L1 -- Acorda LMB 9 -- Battelle Memorial Institute, NIH L-761191 -- Merck lactoferrin – Meristem, Pharming, Agennix LM-CD45 -- Cantab Pharmaceuticals lactoferrin cardio - Pharming lovastatin -- Merck LSA-3 LAG-3 -- Serono LT-ß receptor -- Biogen LAIT - GEMMA lung cancer vaccine -- Corixa LAK cell cytotoxin -- Arizona lamellarins - PharmaMar/University of lusupultide -- Scios L-Vax -- AVAX Malaga laminin A peptides -- NIH LY 355455 - Eli Lilly LY 366405 -- Eli Lilly lanoteplase -- Genetics Institute LY-355101 -- Eli Lilly Iaronidase -- BioMarin Lyme disease DNA vaccine -- Vical/Aventis Lassa fever vaccine Pasteur LCAT -- NIH Lyme disease vaccine -- Aquila LDP 01 -- Millennium LDP 02 -- Millennium Biopharmaceuticals, Aventis, Pasteur, Symbicom, GlaxoSmithKline, Hyland Lecithinized superoxide dismutase --Immuno. Medimmune Seikagaku Lymphocytic choriomeningitis virus vaccine LelF adjuvant -- Corixa lymphoma vaccine - Biomira, Genitope leishmaniasis vaccine --- Corixa LYP18 lenercept -- Hoffman La-Roche lys plasminogen, recombinant Lenograstim -- Aventis, Chugai Lysosomal storage disease gene therapy -lepirudin -- Aventis leptin - Amgen, IC Innovations Avigen lysostaphin -- Nutrition 21 Leptin gene therapy -- Chiron Corporation

FIG. 28Q

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MEDI 507 - BioTransplant M 23 -- Gruenenthal M1 monoclonal antibodies -- Acorda melanin concentrating hormone --Neurocrine Biosciences Therapeutics MA 16N7C2 - Corvas Intl. melanocortins - OMRF malaria vaccine -- GlaxoSmithKline. Melanoma monoclonal antibodies -- Viragen melanoma vaccine -- GlaxoSmithKline, AdProTech, Antigenics, Apovia, Aventis Pasteur, Axis Genetics, Behringwerke, Akzo Nobel, Avant, Aventis Pasteur, Bavarian Nordic, Biovector, CancerVax, CDCP, Chiron Vaccines, Genzyme Transgenics, Hawaii, MedImmune, NIH. Genzyme Molecular Oncology, Humbolt, NYU, Oxxon, Roche/Saramane, Biotech ImClone Systems, Memorial, NYU, Oxxon Melanoma vaccine Magevac -- Therion Australia, Rx Tech Malaria vaccine CDC/NIIMALVAC-1 memory enhancers -- Scios meningococcal B vaccine -- Chiron malaria vaccine.multicomponent meningococcal vaccine -- CAMR mammaglobin -- Corixa Meningococcal vaccine group B conjugate mammastatin -- Biotherapeutics - North American Vaccine mannan-binding lectin -- Natlmmu mannan-MUC1 -- Psiron Meningococcal vaccine group B recombinant -- BioChem Vaccines, MAP 30 Microscience Marinovir -- Phytera Meningococcal vaccine group Y conjugate -MARstem -- Maret - North American Vaccine MB-015 - Mochida Meningococcal vaccine groups A B and C MBP -- ImmuLogic conjugate -- North American Vaccine MCI-028 -- Mitsubishi-Tokyo Mepolizumab - GlaxoSmithKline MCIF - Human Genome Sciences MDC -- Advanced BioScience -- Akzo Metastatin - EntreMed, Takeda Met-CkB7 -- Human Genome Sciences Nobel, ICOS met-enkephalin -- TNI MDX 11 -- Medarex METH-1 – Human Genome Sciences MDX 210 -- Medarex methioninase - AntiCancer MDX 22 -- Medarex Methionine lyase gene therapy --MDX 22 MDX 240 -- Medarex AntiCancer Met-RANTES - Genexa Biomedical, MDX 33 MDX 44 - Medarex Serono Metreleptin MDX 447 -- Medarex Microtubule inhibitor MAb MDX H210 - Medarex MDX RA -- Houston BioTech., Medarex Immunogen/Abgenix MGDF - Kirin ME-104 - Pharmexa MGV - Progenics Measles vaccine micrin -- Endocrine Mecasermin -- Cephalon/Chiron, Chiron microplasmin -- ThromboGenics MEDI 488 -- Medimmune MIF -- Genetics Institute MEDI 500

FIG. 28R

MAb 45-2D9- - haematoporphyrin migration inhibitory factor -- NIH Mim CD4.1 - Xycte Therapies conjugate mirostipen -- Human Genome Sciences MAb 4B4 Mitumomab (BEC-2) - ImClone Systems, MAb 4E3-CPA conjugate -- BCM Oncologia MAb 4E3-daunorubicin conjugate Merck KGaA MK 852 - Merck MAb 50-6 MAb 50-61A - Institut Pasteur MLN 1202 (Anti-CCR2 monoclonal antibody) - Millenium Pharmaceuticals MAb 5A8 - Biogen MAb 791T/36-methotrexate conjugate Mobenakin - NIS molgramostim - Genetics Institute, Novartis MAb 7c11.e8 monoclonal antibodies -- Abgenix/Celltech, MAb 7E11 C5-selenocystamine conjugate Immusol/ Medarex, Viragen/ Roslin MAb 93KA9 - Novartis Institute, Cambridge Antibody Tech./Elan MAb A5B7-cisplatin conjugate --Biodynamics Research, Pharmacia MAb 108 --MAb A5B7-I-131 MAb 10D5 -MAb 14.18-interleukin-2 immunocytokine - MAb A7 MAb A717 -- Exocell Lexigen MAb A7-zinostatin conjugate MAb 14G2a -MAb ABX-RB2 -- Abgenix MAb 15A10 -MAb, ACA 11 MAb 170 -- Biomira MAb AFP-I-131 - Immunomedics MAb 177Lu CC49 --MAb AP1 MAb 17F9 MAb AZ1 MAb 1D7 MAb B3-LysPE40 conjugate MAb 1F7 – Immune Network MAb B4 - United Biomedical MAb 1H10-doxorubicin conjugate MAb B43 Genistein-conjugate MAb 26-2F MAb B43.13-Tc-99m -- Biomira MAb 2A11 MAb B43-PAP conjugate MAb 2E1 -- RW Johnson MAb B4G7-gelonin conjugate MAb 2F5 MAb BCM 43-daunorubicin conjugate -MAb 31.1 — International BioImmune **BCM Oncologia** MAb BIS-1 MAb 32 - Cambridge Antibody Tech., MAb BMS 181170 -- Bristol-Myers Squibb Peptech MAb BR55-2 MAb 323A3 -- Centocor MAb BW494 MAb 3C5 MAb C 242-DM1 conjugate -- ImmunoGen MAb 3F12 MAb C242-PE conjugate MAb 3F8 MAb c30-6 MAb 42/6 MAb CA208-cytorhodin-S conjugate --MAb 425 - Merck KGaA Hoechst Japan MAb 447-52D - Merck Sharp & Dohme MAb CC49 -- Enzon

FIG. 28S

MAb LL2-I-131 — Immunomedics MAb ch14.18 --MAb CH14.18-GM-CSF fusion protein --MAb LL2-Y-90 MAb LS2D617 -- Hybritech Lexigen MAb chCE7 MAb LYM-1-gelonin conjugate MAb CI-137 -- AMRAD MAb LYM-1-I-131 MAb LYM-1-Y-90 MAb cisplatin conjugate MAb CLB-CD19 MAb LYM-2 -- Peregrine MAb CLB-CD19v MAb M195 MAb M195-bismuth 213 conjugate -MAb CLL-1 -- Peregrine MAb CLL-1-GM-CSF conjugate Protein Design Labs MAb CLL-1-IL-2 conjugate -- Peregrine MAb M195-gelonin conjugate MAb M195-I-131 MAb CLN IgG -- doxorubicin conjugates MAb conjugates – Tanox MAb M195-Y-90. MAb MA 33H1 - Sanofi MAb D612 MAb Dal B02 MAb MAD11 MAb DC101 - ImClone MAb MGb2 MAb MINT5 MAb EA 1 --MAb EC708 -- Biovation MAb MK2-23 MAb EP-5C7 -- Protein Design Labs MAb MOC31 ETA(252-613) conjugate MAb MOC-31-In-111 MAb ERIC-1 -- ICRT MAb MOC-31-PE conjugate MAb F105 gene therapy MAb FC 2.15 MAb MR6 --MAb MRK-16 - Aventis Pasteur MAb G250 -- Centocor MAb GA6 MAb MS11G6 MAb MX-DTPA BrE-3 MAb GA733 MAb Gliomab-H -- Viventia Biotech MAb MY9 MAb Nd2 -- Tosoh MAb HB2-saporin conjugate MAb NG-1 -- Hygeia MAb HD 37 -MAb HD37-ricin chain-A conjugate MAb NM01 - Nissin Food **MAb OC 125** MAb HNK20 -- Acambis MAb OC 125-CMA conjugate MAb huN901-DM1 conjugate --MAb OKI-1 -- Ortho-McNeil ImmunoGen MAb I-131 CC49 -- Corixa MAb OX52 — Bioproducts for Science MAb PMA5 MAb ICO25 MAb PR1 MAb ICR12-CPG2 conjugate MAb prost 30 MAb ICR-62 MAb IRac-ricin A conjugate MAb R-24 MAb K1 MAb R-24 a Human GD3 -- Celltech MAb RFB4-ricin chain A conjugate MAb KS1-4-methotrexate conjugate MAb L6 -- Bristol-Myers Squibb, Oncogen MAb RFT5-ricin chain A conjugate MAb LiCO 16-88 MAb SC 1

FIG. 28T

Muc-1 vaccine -- Corixa MAb SM-3 -- ICRT MAb SMART 1D10 -- Protein Design Labs mucosal tolerance -- Aberdeen mullerian inhibiting subst MAb SMART ABL 364 - Novartis muplestim -- Genetics Institute, Novartis, MAb SN6f MAb SN6f-deglycosylated ricin A chain DSM Anti-Infectives murine MAb -- KS Biomedix conjugate -Mutant somatropin -- JCR Pharmaceutical MAb SN6i MV 833 -- Toagosei MAb SN7-ricin chain A conjugate Mycoplasma pulmonis vaccine MAb T101-Y-90 conjugate -- Hybritech Mycoprex -- XOMA MAb T-88 -- Chiron myeloperoxidase - Henogen MAb TB94 -- Cancer ImmunoBiology myostatin -- Genetics Institute MAb TEC 11 Nacolomab tafenatox -- Pharmacia MAb TES-23 -- Chugai Nagrecor -- Scios MAb TM31 -- Avant MAb TNT-1 -- Cambridge Antibody Tech., nagrestipen -- British Biotech NAP-5 - Corvas Intl. Peregrine NAPc2 – Corvas Intl. MAb TNT-3 nartograstim -- Kyowa MAb TNT-3 -- IL2 fusion protein --Natalizumab -- Protein Design Labs MAb TP3-At-211 Nateplase - NIH, Nihon Schering MAb TP3-PAP conjugate nateplase -- Schering AG MAb UJ13A -- ICRT NBI-3001 -- Neurocrine Biosci. MAb UN3 NBI-5788 -- Neurocrine Biosci. MAb ZME-018-gelonin conjugate NBI-6024 — Neurocrine Biosci. MAb-BC2 - GlaxoSmithKline Nef inhibitors -- BRI MAb-DM1 conjugate -- ImmunoGen Neisseria gonorrhoea vaccine -- Antex MAb-ricin-chain-A conjugate -- XOMA Biologics MAb-temoporfin conjugates Neomycin B-arginine conjugate Monopharm C -- Viventia Biotech Nerelimomab -- Chiron monteplase -- Eisai Nerve growth factor - Amgen -- Chiron, montirelin hydrate - Gruenenthal Genentech moroctocog alfa - Genetics Institute Nerve growth factor gene therapy Moroctocog-alfa -- Pharmacia nesiritide citrate -- Scios MP 4 neuregulin-2 -- CeNeS MP-121 -- Biopharm neurocan -- NYU MP-52 -- Biopharm neuronal delivery system -- CAMR MRA -- Chugai Neurophil inhibitory Factor -- Corvas MS 28168 -- Mitsui Chemicals, Nihon Neuroprotective vaccine -- University of Schering Auckland MSH fusion toxin -- Ligand neurotrophic chimaeras -- Regeneron MSI-99 -- Genaera neurotrophic factor -- NsGene, CereMedix MT 201 -- Micromet

FIG. 28U

NeuroVax -- Immune Response Oncophage -- Antigenics Oncostatin M -- Bristol-Myers Squibb neurturin - Genentech OncoVax-CL -- Jenner Biotherapies neutral endopeptidase - Genentech OncoVax-P -- Jenner Biotherapies NGF enhancers -- NeuroSearch NHL vaccine -- Large Scale Biology onercept -- Yeda NIP45 - Boston Life Sciences onychomycosis vaccine -- Boehringer Inaelheim NKI-B20 opebecan - XOMA NM 01 - Nissin Food opioids -- Arizona NMI-139 -- NitroMed Oprelvekin – Genetics Institute NMMP -- Genetics Institute Oregovomab -- AltaRex NN-2211 -- Novo Nordisk Org-33408 b- Akzo Nobel Noggin - Regeneron Orolip DP -- EpiCept Nonacog alfa oryzacystatin Norelin -- Biostar OSA peptides – GenSci Regeneration Norwalk virus vaccine osteoblast-cadherin GF -- Pharis NRLU 10 -- NeoRx Osteocalcin-thymidine kinase gene therapy NRLU 10 PE -- NeoRx osteogenic protein -- Curis NT-3 -- Regeneron osteopontin -- OraPharma NT-4/5 -- Genentech osteoporosis peptides -- Integra, Telios NU 3056 osteoprotegerin - Amgen, SnowBrand NU 3076 otitis media vaccines - Antex Biologics NX 1838 -- Gilead Sciences ovarian cancer -- University of Alabama NY ESO-1/CAG-3 antigen -- NIH OX40-IgG fusion protein -- Cantab, Xenova NYVAC-7 -- Aventis Pasteur P 246 -- Diatide NZ-1002 -- Novazyme P 30 -- Alfacell obesity therapy - Nobex p1025 - Active Biotech OC 10426 -- Ontogen P-113[^] - Demegen OC 144093 -- Ontogen P-16 peptide -- Transition Therapeutics OCIF -- Sankyo p43 -- Ramot Oct-43 -- Otsuka P-50 peptide - Transition Therapeutics Odulimomab - Immunotech p53 + RAS vaccine -- NIH, NCI OK PSA - liposomal PACAP(1-27) analogue OKT3-gamma-1-ala-ala paediatric vaccines -- Chiron OM 991 Pafase - ICOS OM 992 PAGE-4 plasmid DNA -- IDEC Omalizumab -- Genentech PAI-2 -- Biotech Australia, Human oncoimmunin-L -- NIH Therapeutics. Oncolysin B -- ImmunoGen Palifermin (keratinocyte growth factor) --Oncolysin CD6 -- ImmunoGen Amgen Oncolysin M -- ImmunoGen Palivizumab -- MedImmune Oncolvsin S -- ImmunoGen

FIG. 28V

PEG-uricase -- Mountain View PAM 4 -- Merck Pegvisomant -- Genentech pamiteplase - Yamanouchi PEGylated proteins, PolyMASC -- Valentis pancreatin, Minitabs -- Eurand PEGylated recombinant native human leptin Pangen -- Fournier Pantarin - Selective Genetics -- Roche Parainfluenza virus vaccine - Pharmacia, Pemtumomab Penetratin -- Cyclacel Pierre Fabre Pepscan - Antisoma paraoxanase -- Esperion parathyroid hormone - Abiogen, Korea peptide G - Peptech, ICRT peptide vaccine - NIH ,NCl **Green Cross** Pexelizumab Parathyroid hormone (1-34) -pexiganan acetate -- Genaera Chugai/Suntory Pharmaprojects No. 3179 -- NYU Parkinson's disease gene therapy -- Cell Pharmaprojects No. 3390 -- Ernest Orlando Genesys/ Ceregene Pharmaprojects No. 3417 -- Sumitomo Parvovirus vaccine -- MedImmune Pharmaprojects No. 3777 -- Acambis PCP-Scan - Immunomedics Pharmaprojects No. 4209 -- XOMA PDGF -- Chiron Pharmaprojects No. 4349 – Baxter Intl. PDGF cocktail -- Theratechnologies Pharmaprojects No. 4651 peanut allergy therapy - Dynavax Pharmaprojects No. 4915 -- Avanir PEG anti-ICAM MAb -- Boehringer Pharmaprojects No. 5156 -- Rhizogenics Ingelheim Pharmaprojects No. 5200 -- Pfizer PEG asparaginase -- Enzon · Pharmaprojects No. 5215 -- Origene PEG glucocerebrosidase Pharmaprojects No. 5216 -- Origene PEG hirudin -- Knoll Pharmaprojects No. 5218 - Origene PEG interferon-alpha-2a -- Roche Pharmaprojects No. 5267 -- ML PEG interferon-alpha-2b + ribavirin -Laboratories Biogen, Enzon, ICN Pharmaceuticals, Pharmaprojects No. 5373 -- MorphoSys Schering-Plough Pharmaprojects No. 5493 -- Metabolex PEG MAb A5B7 -Pharmaprojects No. 5707 -- Genentech Pegacaristim - Amgen -- Kirin Brewery --Pharmaprojects No. 5728 -- Autogen ZymoGenetics Pharmaprojects No. 5733 -- BioMarin Pegaldesleukin -- Research Corp Pharmaprojects No. 5757 -- NIH pegaspargase -- Enzon Pharmaprojects No. 5765 -- Gryphon pegfilgrastim -- Amgen Pharmaprojects No. 5830 -- AntiCancer PEG-interferon Alpha -- Viragen Pharmaprojects No. 5839 -- Dyax PEG-interferon Alpha 2A -- Hoffman La-Pharmaprojects No. 5849 -- Johnson & Roche Johnson PEG-interferon Alpha 2B -- Schering-Pharmaprojects No. 5860 -- Mitsubishi-Plough Tokyo PEG-r-hirudin -- Abbott PEG-rHuMGDF -- Amgen

FIG. 28W

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Plasminogen activators -- Abbott Pharmaprojects No. 5869 -- Oxford Laboratories, American Home Products, GlycoSciences Boehringer Mannheim, Chiron Pharmaprojects No. 5883 - Asahi Brewery Pharmaprojects No. 5947 -- StressGen Corporation, DuPont Pharmaceuticals, Eli Lilly, Shlonogi, Genentech, Genetics Pharmaprojects No. 5961 --Institute, GlaxoSmithKline, Hemispherx Theratechnologies Pharmaprojects No. 5962 - NIH Biopharma, Merck & Co, Novartis, Pharmacia Corporation, Wakamoto, Yeda Pharmaprojects No. 5966 -- NIH plasminogen-related peptides -- Bio-Tech. Pharmaprojects No. 5994 - Pharming Pharmaprojects No. 5995 -- Pharming General/MGH Pharmaprojects No. 6023 - IMMUCON platelet factor 4 -- RepliGen Platelet-derived growth factor - Amgen --Pharmaprojects No. 6063 - Cytoclonal ZymoGenetics Pharmaprojects No. 6073 -- SIDDCO plusonermin-- Hayashibara Pharmaprojects No. 6115 -- Genzyme PMD-2850 -- Protherics Pharmaprojects No. 6227 -- NIH Pneumococcal vaccine -- Antex Biologics, Pharmaprojects No. 6230 -- NIH Aventis Pasteur Pharmaprojects No. 6236 -- NIH Pneumococcal vaccine intranasal --Pharmaprojects No. 6243 -- NIH BioChem Vaccines/Biovector Pharmaprojects No. 6244 -- NIH PR1A3 Pharmaprojects No. 6281 - Senetek PR-39 Pharmaprojects No. 6365 – NIH pralmorelin -- Kaken Pharmaprojects No. 6368 -- NIH Pretarget-Lymphoma -- NeoRx Pharmaprojects No. 6373 -- NIH Priliximab -- Centocor Pharmaprojects No. 6408 -- Pan Pacific PRO 140 -- Progenics Pharmaprojects No. 6410 – Athersys PRO 2000 -- Procept Pharmaprojects No. 6421 -- Oxford **GlycoSciences** PRO 367 -- Progenics PRO 542 -- Progenics Pharmaprojects No. 6522 -- Maxygen pro-Apo A-I -- Esperion Pharmaprojects No. 6523 -- Pharis prolactin -- Genzyme Pharmaprojects No. 6538 -- Maxygen Pharmaprojects No. 6554 - APALEXO Prosaptide TX14(A) -- Bio-Tech. General prostate cancer antbodies -- Immunex, Pharmaprojects No. 6560 -- Ardana Pharmaprojects No. 6562 -- Bayer **UroCor** prostate cancer antibody therapy --Pharmaprojects No. 6569 -- Eos Genentech/UroGenesys. Phenoxazine Phenylase -- Ibex Genotherapeutics prostate cancer immunotherapeutics -- The Pigment epithelium derived factor --**PSMA Development Company** plasminogen activator inhibitor-1, prostate cancer vaccine -- Aventis Pasteur, recombinant -- DuPont Pharmaceuticals --Zonagen, Corixa, Dendreon, Jenner Biotheraples, Therion Biologics

FIG. 28X

RD 62198 prostate-specific antigen -- EntreMed rDnase -- Genentech protein A -- RepliGen RDP-58 -- SangStat protein adhesives -- Enzon protein C -- Baxter Intl., PPL Therapeutics, RecepTox-Fce - Keryx RecepTox-GnRH - Keryx, MTR ZvmoGenetics **Technologies** protein C activator – Gilead Sciences RecepTox-MBP - Keryx, MTR protein kinase R antags -- NIH **Technologies** protirelin - Takeda protocadherin 2 -- Caprion recFSH -- Akzo Nobel, Organon REGA 3G12 Pro-urokinase - Abbott, Bristol-Myers Squibb, Dainippon, Tosoh -- Welfide Regavirumab - Teijin P-selectin glycoprotein ligand-1 -- Genetics relaxin -- Connetics Corp Renal cancer vaccine -- Macropharm Institute pseudomonal infections -- InterMune repifermin -- Human Genome Sciences Respiratory syncytial virus PFP-2 vaccine --Pseudomonas vaccine - Cytovax Wyeth-Lederle PSGL-Ig -- American Home Products Respiratory syncytial virus vaccine --PSP-94 -- Procyon GlaxoSmithKline, Pharmacia, Pierre Fabre PTH 1-34 -- Nobex Respiratory syncytial virus vaccine Quilimmune-M -- Antigenics inactivated R 744 -- Roche Respiratory syncytial virus-parainfluenza R 101933 virus vaccine -- Aventis Pasteur, R 125224 -- Sankyo Pharmacia RA therapy -- Cardion Rabies vaccine recombinant -- Aventis Reteplase - Boehringer Mannheim, Hoffman La-Roche Pasteur, BioChem Vaccines, Kaketsuken Retropep -- Retroscreen **Pharmaceuticals** RadioTheraClM -- YM BioSciences RFB4 (dsFv) PE38 RFI 641 - American Home Products Ramot project No. 1315 -- Ramot RFTS – UAB Research Foundation Ramot project No. K-734A - Ramot RG 12986 -- Aventis Pasteur Ramot project No. K-734B -- Ramot RG 83852 -- Aventis Pasteur Ranibizumab (Anti-VEGF fragment) --RG-1059 - RepliGen Genentech rGCR -- NIH RANK -- Immunex ranpirnase -- Alfacell rGLP-1 -- Restoragen ranpirnase-anti-CD22 MAb -- Alfacell rGRF -- Restoragen rh Insulin - Eli Lilly RANTES inhibitor — Milan RHAMM targeting peptides - Cangene RAPID drug delivery systems - ARIAD rHb1.1 - Baxter Intl. rasburicase -- Sanofi rBPI-21, topical -- XOMA rhCC10 - Claragen RC 529 -- Corixa rhCG - Serono · Rheumatoid arthritis gene therapy rCFTR - Genzyme Transgenics

FIG. 28Y

SB RA 31012 -Rheumatoid arthritis vaccine -- Veterans SC 56929 - Pharmacia Affairs Medical Center SCA binding proteins -- Curis, Enzon rhLH -- Serono scFv(14E1)-ETA Berlex Laboratories, Ribozyme gene therapy -- Genset Schering AG Rickettsial vaccine recombinant ScFv(FRP5)-ETA -RIGScan CR -- Neoprobe ScFv6C6-PE40 -RIP-3 -- Rigel SCH 55700 -- Celltech Rituximab -- Genentech Schistosomiasis vaccine -- Glaxo RK-0202 -- RxKinetix Wellcome/Medeva, Brazil RLT peptide -- Esperion SCPF -- Advanced Tissue Sciences rM/NEI -- IVAX scuPA-suPAR complex -- Hadasit rmCRP -- Immtech SD-9427 -- Pharmacia RN-1001 -- Renovo SDF-1 -- Ono RN-3 -- Renovo SDZ 215918 - Novartis RNAse conjugate -- Immunomedics SDZ 280125 -- Novartis RO 631908 -- Roche SDZ 89104 -- Novartis Rotavirus vaccine -- Merck SDZ ABL 364 -- Novartis RP 431 -- DuPont Pharmaceuticals SDZ MMA 383 -- Novartis RP-128 -- Resolution Secretin - Ferring, Repligen RPE65 gene therapy -serine protease inhibs -- Pharis RPR 110173 -- Aventis Pasteur sermorelin acetate -- Serono RPR 115135 -- Aventis Pasteur SERP-1 -- Viron RPR 116258A -- Aventis Pasteur sertenef - Dainippon rPSGL-Ig -- American Home Products serum albumin, Recombinant human r-SPC surfactant -- Byk Gulden **Aventis Behring** RSV antibody -- Medimmune serum-derived factor -- Hadasit Ruplizumab -- Biogen: Sevirumab -- Novartis rV-HER-2/neu -- Therion Biologics SGN 14 - Seatle Genetics SA 1042 -- Sankyo SGN 15 - Seatle Genetics sacrosidase -- Orphan Medical SGN 17/19 - Seatle Genetics SGN 30 - Seatle Genetics Sargramostim -- Immunex SGN-10 - Seatle Genetics saruplase -- Gruenenthal SGN-11 - Seatle Genetics Satumomab -- Cytogen SH 306 - DuPont Pharmaceuticals SB 1 - COR Therapeutics Shanvac-B -- Shantha SB 207448 - GlaxoSmithKline Shigella flexneri vaccine - Avant, Acambis, SB 208651 — GlaxoSmithKline Novavax SB 240683 -- GlaxoSmithKline Shigella sonnei vaccine -SB 249415 -- GlaxoSmithKline sICAM-1 -- Boehringer ingelheim SB 249417 -- GlaxoSmithKline Silteplase -- Genzyme SB 6 - COR Therapeutics

FIG. 28Z

Staphylococcus aureus vaccine conjugate --SIV vaccine - Endocon, Institut Pasteur SK 896 -- Sanwa Kagaku Kenkyusho Staphylococcus therapy - Tripep SK-827 - Sanwa Kagaku Kenkyusho Staphylokinase - Biovation, Prothera, Skeletex - CellFactors Thrombogenetics SKF 106160 - GlaxoSmithKline Streptococcal A vaccine -- M6 S-nitroso-AR545C --Pharmaceuticals, North American Vaccine SNTP - Active Biotech Streptococcal B vaccine -- Microscience somatomedin-1 - GroPep, Mitsubishi-Streptococcal B vaccine recombinant --Tokyo, NIH Biochem Vaccines somatomedin-1 carrier protein -- Insmed Streptococcus pyogenes vaccine somatostatin -- Ferring STRL-33 -- NIH Somatotropin/ Subalin -- SRC VB VECTOR Human Growth Hormone -- Bio-Tech. SUIS -- United Biomedical General, Eli Lilly somatropin -- Bio-Tech. General, Alkermes, SUIS-LHRH - United Biomedical ProLease, Aventis Behring, Biovector, SUN-E3001 -- Suntory super high affinity monoclonal antibodies --Cangene, Dong-A, Eli Lilly, Emisphere, Enact, Genentech, Genzyme Transgenics, YM BioSciences Grandis/InfiMed, CSL, InfiMed, MacroMed, Superoxide dismutase - Chiron, Enzon, Ube Industries, Bio-Tech, Yeda Novartis, Novo Nordisk, Pharmacia superoxide dismutase-2 -- OXIS Serono, TranXenoGen suppressin -- UAB Research Foundation somatropin derivative - Schering AG SY-161-P5 -- ThromboGenics somatropin, AIR -- Eli Lilly SY-162 -- ThromboGenics Somatropin, inhaled - Eli Lilly/Alkermes Systemic lupus erythematosus vaccine -somatropin, Kabi -- Pharmacia MedClone/VivoRx somatropin, Orasome -- Novo Nordisk T cell receptor peptides -- Xoma Sonermin - Dainippon Pharmaceutical T cell receptor peptide vaccine SP(V5.2)C - Supertek T4N5 liposomes -- AGI Dermatics SPf66 TACI, soluble -- ZymoGenetics sphingomyelinase - Genzyme targeted apoptosis -- Antisoma SR 29001 - Sanofi tasonermin -- Boehringer Ingelheim SR 41476 -- Sanofi TASP SR-29001 - Sanofi TASP-V SS1(dsFV)-PE38 - NeoPharm Tat peptide analogues -- NIH ß2 microglobulin -- Avidex TBP I -- Yeda ß2-microglobulin fusion proteins -- NIH TBP II ß-amyloid peptides - CeNeS TBV25H - NIH ß-defensin -- Pharis Tc 99m ior cea1 — Center of Molecular Staphylococcus aureus infections -**Immunology** Inhibitex/ZLB Tc 99m P 748 -- Diatide

FIG. 28AA

TIF -- Xoma

Tifacogin -- Chiron, NIS, Pharmacia

58/497

Tissue factor - Genentech Tc 99m votumumab -- Intracell Tc-99m rh-Annexin V - Theseus Imaging Tissue factor pathway inhibitor TJN-135 - Tsumura teceleukin -- Biogen TM 27 -- Avant tenecteplase - Genentech Teriparatide -- Armour Pharmaceuticals, TM 29 - Avant TMC-151 - Tanabe Seiyaku Asahi Kasei, Eli Lilly TNF tumour necrosis factor -- Asahi Kasei terlipressin -- Ferring TNF Alpha -- Cytlmmune testisin -- AMRAD TNF antibody -- Johnson & Johnson Tetrafibricin -- Roche TNF binding protein -- Amgen TFPI -- EntreMed TNF degradation product - Oncotech to D-IL-2 - Takeda TNF receptor - Immunex TGF-Alpha -- ZymoGenetics TNF receptor 1, soluble -- Amgen TGF-ß -- Kolon TNF Tumour necrosis factor-alpha -- Asahi TGF-B2 -- Insmed Kasei, Genetech, Mochida TGF-ß3 -- OSI TNF-Alpha inhibitor -- Tripep Thalassaemia gene therapy -- Crucell TNFR:Fc gene therapy -- Targeted Genetics TheraClM-h-R3 -- Center of Molecular Immunology, YM BioSciences TNF-SAM2 ToleriMab -- Innogenetics Theradigm-HBV -- Epimmune Toxoplasma gondii vaccine – Theradigm-HPV -- Epimmune GlaxoSmithKline Theradigm-malaria -- Epimmune TP 9201 -- Telios Theradigm-melanoma -- Epimmune TP10 -- Avant TheraFab -- Antisoma ThGRF 1-29 -- Theratechnologies TP20 -- Avant ThGRF 1-44 -- Theratechnologies tPA -- Centocor Thrombin receptor activating peptide -trafermin -- Scios TRAIL/Apo2L -- Immunex Abbott TRAIL-R1 MAb - Cambridge Antibody thrombomodulin -- Iowa, Novocastra Thrombopoietin - Dragon Pharmaceuticals, Technologies transferrin-binding proteins - CAMR Genentech Transforming growth factor-beta-1 -thrombopoietin, Pliva -- Receptron Genentech Thrombospondin 2 – transport protein -- Genesis thrombostatin - Thromgen Trastuzumab -- Genetech thymalfasin - SciClone TRH -- Ferring thymocartin - Gedeon Richter thymosin Alpha1 -- NIH Triabin -- Schering AG Triconal · thyroid stimulating hormone - Genzyme Triflavin tICAM-1 -- Bayer troponin I - Boston Life Sciences Tick anticoagulant peptide - Merck

FIG. 28BB

TRP-2[^] -- NIH

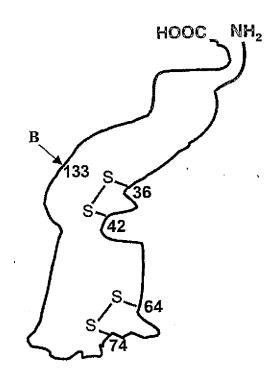
trypsin inhibitor - Mochida

Vascular endothelial growth factors - R&D TSP-1 gene therapy -Systems TT-232 vascular targeting agents - Peregrine TTS-CD2 -- Active Biotech vasopermeation enhancement agents --Tuberculosis vaccine - Aventis Pasteur, Peregrine Genesis vasostatin - NIH Tumor Targeted Superantigens – Active VCL - Bio-Tech, General Biotech -- Pharmacia VEGF - Genentech, Scios tumour vaccines -- PhotoCure tumour-activated prodrug antibody VEGF inhibitor -- Chugai conjugates - Millennium/ImmunoGen VEGF-2 -- Human Genome Sciences VEGF-Trap -- Regeneron tumstatin -- ILEX viscumin, recombinant - Madaus Tuvirumab -- Novartis Vitaxin TV-4710 – Teva Vitrase -- ISTA Pharmaceuticals TWEAK receptor -- Immunex West Nile virus vaccine -- Bavarian Nordic TXU-PAP WP 652 TY-10721 – TOA Eiyo WT1 vaccine -- Corixa Type I diabetes vaccine -- Research Corp WX-293 - Wilex BioTech. Typhoid vaccine CVD 908 WX-360 -- Wilex BioTech. U 143677 -- Pharmacia WX-UK1 - Wilex BioTech. U 81749 -- Pharmacia XMP-500 -- XOMA UA 1248 -- Arizona XomaZyme-791 -- XOMA UGIF - Sheffield XTL 001 - XTL Biopharmaceuticals UIC 2 XTL 002 -- XTL Biopharmaceuticals UK 101 yeast delivery system -- Globelmmune UK-279276 -- Corvas Intl. Yersinia pestis vaccine urodilatin - Pharis YIGSR-Stealth -- Johnson & Johnson urofollitrophin - Serono Yissum Project No. D-0460 -- Yissum Urokinase -- Abbott YM 207 - Yamanouchi uteroferrin-- Pepgen YM 337 -- Protein Design Labs V 20 -- GLYCODesign Yttrium-90 labelled biotin V2 vasopressin receptor gene therapy Yttrium-90-labeled anti-CEA MAb T84.66 vaccines -- Active Biotech ZD 0490 – AstraZeneca Varicella zoster glycoprotein vaccine -ziconotide -- Elan Research Corporation Technologies Varicella zoster virus vaccine livé -- Cantab ZK 157138 -- Berlex Laboratories Zolimomab aritox **Pharmaceuticals** Zorcell - Immune Response Vascular endothelial growth factor -

FIG. 28CC

Genentech, University of California

ZRXL peptides -- Novartis



$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{Sia})_b \\ -\operatorname{GalNAc-(Gal)}_a - (\operatorname{Sia})_c - (R)_d \end{pmatrix}_e$$

a-c, e (independently selected) = 0 or 1; d = 0; R = modifying group, sialyl or oligosialyl

FIG. 29A

CHO, BHK, 293 cells, Vero expressed G-CSF a-c, e (independently selected) = 0 or 1; d = 0

- Sialidase
 - 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 29B

Insect cell expressed G-CSF a, e (independently selected) = 0 or 1; b, c, d = 0.

- 1. Galactosyltransferase, UDP-Gal
 2. CMP-SA-PEG, ST3Gal1
- a, c, d, e (independently selected) = 0 or 1; R = PEG.

FIG. 29C

E. coli expressed G-CSF a-e=0.

- 1. GalNAc Transferase, UDP-GalNAc

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 29D

NSO expressed G-CSF a, e (independently selected) = 0 or 1; b, c, d = 0

- 1. CMP-SA-levulinate, ST3Gal1
 2. H₄N₂-PEG
- a, c, d, e (independently selected) = 0 or 1; b = 0; R = PEG.

FIG. 29E

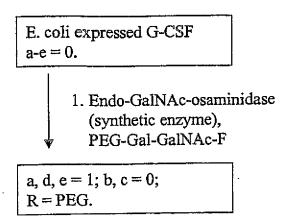


FIG. 29F

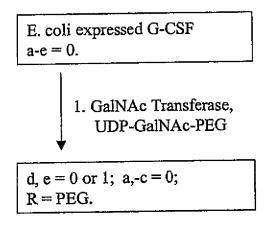
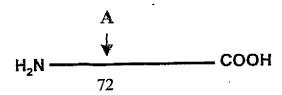


FIG. 29G



$$\mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_a]_e - (\mathrm{Sia})_j - (\mathrm{R})_v \end{bmatrix}_r \\ [\mathrm{GlcNAc} - (\mathrm{Gal})_b]_f - (\mathrm{Sia})_k - (\mathrm{R})_w \end{bmatrix}_s \\ [\mathrm{GlcNAc} - (\mathrm{Gal})_c]_g - (\mathrm{Sia})_l - (\mathrm{R})_x \end{bmatrix}_t \\ [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_c]_g - (\mathrm{Sia})_l - (\mathrm{R})_x \end{bmatrix}_t \\ [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{R})_y \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Sia})_m - (\mathrm{Gal})_d \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Gal})_d \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Gal})_d \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Gal})_d \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Gal})_d \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Gal})_d \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Gal})_d \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Gal})_d \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Gal})_d \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Gal})_d \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc} - (\mathrm{Gal})_d]_h - (\mathrm{Gal})_d \end{bmatrix}_u \\ \mathbf{A} \leftarrow \begin{bmatrix} [$$

a-d, i, n-u (independently selected) = 0 or 1.

aa, bb, cc, dd, ee (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 20.

v-z = 0; R = modifying group, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 30A

```
ŒIO, BHK, 293 cells, Vero expressed interferon alpha 14C.
a-d, aa, bb = 1; e-h = 1 to 4;
cc, j-m, i, r-u (independently selected) = 0 or 1;
q, n-p, v-z, cc, dd, ee = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-d, aa, bb = 1; e-h = 1 to 4;
bb, cc, i, r-u (independently selected) = 0 or 1;
q, n-p, v-z, cc, dd, ee = 0;
v-y (independently selected) = 1,
when j-m (independently selected) = 1;
R = PEG.
```

FIG. 30B

```
Insect cell or fungi expressed interferon alpha-14C.
a-d, f, h, j-q, s, u, v-z, cc, dd, ee = 0;
e, g, i, r, t (independently selected) = 0 or 1;
aa, bb = 1.
```

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
b, d, f, h, j-q, s, u, w, y, z, cc, dd, ee = 0;
a, c, e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when a, c, (independently selected) = 1;
aa, bb = 1; R = PEG.
```

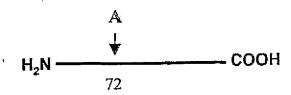
FIG. 30C

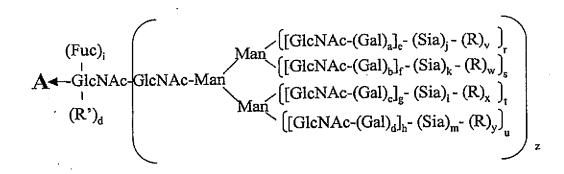
Yeast expressed interferon alpha-14C. a-q, cc, dd, ee, v-z = 0; r-y (independently selected) = 0 to 1; aa, bb = 1;R (branched or linear) = Man, oligomannose or polysaccharide.

- 1. Endo-H
- Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal3

a-z, bb = 0; aa = 1; R' = -Gal-Sia-PEG.

FIG. 30D





a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1. R = polymer; R' = sugar, glycoconjugate.

FIG. 30E

```
CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.

h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.
```

1. CMP-SA-PEG, ST3Gal3

```
h = 1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.
```

FIG. 30F

```
Insect cell or fungi expressed
interferon alpha-14C.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0 or 1;
z = 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, r-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.
```

FIG. 30G

Yeast expressed interferon alpha-14C. a-n = 0; r-y (independently selected) = 0 to 1; z = 1; R (branched or linear) = Man, oligomannose.

- 1. mannosidases
- 2. GNT's 1,2,4,5, UDP-GlcNAc
- 3. Galactosyltransferase, UDP-Gal
- 4.. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.

FIG. 30H

NSO expressed interferon alpha 14C. a-i, r-u (independently selected) = 0 or 1; j-m, n, v-y = 0; z = 1.

> CMP-SA-levulinate, ST3Gal3, buffer, salt
> 2. H₄N₂-PEG

a-i, j-m, r-y (independently selected) = 0 or 1; n = 0; z = 1; R = PEG.

FIG. 301

```
CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.

h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.
```

1. CMP-SA-PEG, α2,8-ST

```
h = 1 to 3;
a-g, i, r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
z = 1; n = 0; R = PEG.
```

FIG. 30J

```
CHO, BHK, 293 cells, Vero expressed
Interferon alpha-14C.
a-g, j-m, r-u (independently selected) = 0 or 1;
h = 1 to 3; n, v-y = 0; z = 1.
```

- 1. Sialidase
- 2. Trans-sialidase, PEG-Sia-lactose

```
a-g, j-m, r-y (independently selected) = 0 or 1;
h = 1 to 3; n = 0; z = 1; R = PEG.
```

FIG. 30K

```
CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.

h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.

1. CMP-SA, α2,8-ST
```

```
h = 1 to 3;
a-g, i, r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0 to 40;
z = 1; v-y, n = 0.
```

FIG. 30L

```
Insect cell or fungi expressed interferon alpha-14C. a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0 or 1; z = 1.
```

- 1. GNT's 1 & 2, UDP-GlcNAc
- Galactosyltransferase, UDP-Gal-linker-SA-CMP
- 3. ST3Gal3, transferrin

a, c, e, g, i, r, t, v, x (independently selected) = 0 or 1; z = 1; b, d, f, h, j-n, s, u, w, y = 0; R = transferrin.

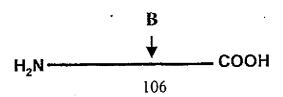
FIG. 30M

```
Insect cell or fungi expressed interferon alpha-14C.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0 or 1; z = 1.
```

- 1. endoglycanase
- 2. Galactosyltransferase, UDP-Gal-linker-SA-CMP
- 3. ST3Gal3, transferrin

```
i (independently selected) = 0 or 1;
a-h, j-m, r-z = 0;
n = 1; R' = -Gal-linker-transferrin.
```

FIG. 30N



$$\mathbf{B} \leftarrow \begin{bmatrix} (\operatorname{GlcNAc-Gal})_{f_c}(\operatorname{Sia})_{b} - (R)_{g} \\ | \\ -\operatorname{GalNAc-(Gal})_{a} - (\operatorname{Sia})_{c} - (R)_{d} \end{bmatrix}_{e}$$

a-c, e, f (independently selected) = 0 or 1; d, g = 0; R = polymer, glycoconjugate.

FIG. 300

CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b).
a-c (independently selected) = 0 or 1;
e = 1; d, f, g = 0

- Sialidase
 - 2. CMP-SA-PEG, ST3Gal1

a-d (independently selected) = 0 or 1; e = 1; b, f, g = 0; R = PEG.

FIG. 30P

Insect cell expressed interferon alpha (2a or 2b). a, e (independently selected) = 0 or 1; b, c, d, f, g = 0.

- 1. Galactosyltransferase, UDP-Gal
 - 2. CMP-SA-PEG, ST3Gal1

a, c, d, e (independently selected) = 0 or 1; b, f, g = 0; R = PEG.

FIG. 30Q

E. coli expressed IF-alpha (2a or 2b). a-g = 0.

 GalNAc Transferase, UDP-GalNAc-PEG

a-c, f, g = 0; d, e = 1; R = PEG.

FIG. 30R

NSO expressed IF-alpha (2a or 2b). a (independently selected) = 0 or 1; e = 1; b, c, d, f, g = 0

1. CMP-SA-levulinate, ST3Gal1

2. H₄N₂-PEG

a, c, d (independently selected) = 0 or 1; e = 1; b, f, g = 0; R = PEG.

FIG. 30S

E. coli expressed IF-alpha (2a or 2b). a-g=0.

 Endo-N-acetylgalatosamidase (synthetic enzyme), PEG-Gal-GalNAc-F

a, d, e = 1; b, c, f, g = 0; R = PEG.

FIG. 30T

E. coli expressed IF-alpha (2a or 2b). a-g = 0.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. sialyltransferase, CMP-SA-PEG

b, d = 0 or 1; e = 1; a, c, f, g = 0; R = PEG.

FIG. 30U

```
CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b).
a-c, f (independently selected) = 0 or 1;
e = 1; d, g = 0
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1 and ST3Gal3

```
a-d, f, g (independently selected) = 0 or 1;
e = 1; R = PEG.
```

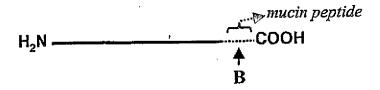
FIG. 30V

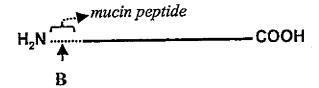
```
CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b). a-c, f (independently selected) = 0 or 1; e = 1; d, g = 0
```

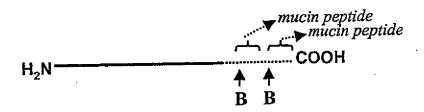
- 1. Sialidase
- CMP-SA-linker-SA-CMP, ,ST3Gal1
- 3. ST3Gal3, transferrin

a-d, f (independently selected) = 0 or 1; e = 1; R = transferrin; g = 0.

FIG. 30W







$$\mathbf{B} \leftarrow \begin{bmatrix} (\operatorname{Sia})_{b} \\ -\operatorname{GalNAc-(Gal)}_{a} - (\operatorname{Sia})_{c} - (R)_{d} \end{bmatrix}_{c}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer, glycoconjugate.

FIG. 30X

CHO, BHK, 293 cells, Vero expressed interferon alpha-mucin fusion protein. a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 30Y

Insect cell expressed interferon alpha-mucin fusion protein.

a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

FIG. 30Z

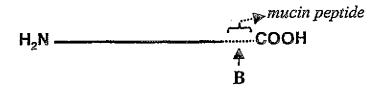
E. coli expressed interferon alpha-mucin fusion protein.

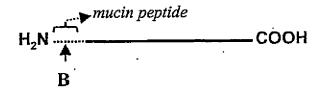
$$a-e = 0$$
.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 30AA





$$\mathbf{B} \quad \leftarrow \begin{bmatrix} (\operatorname{Sia})_{b} \\ & \\ -\operatorname{GalNAc-(Gal)}_{a} - (\operatorname{Sia})_{c} - (R)_{d} \end{bmatrix}_{e}$$

$$\mathbf{C} \leftarrow (\mathbf{R'})_{\mathbf{n}}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer, linker.

FIG. 30BB

E. coli expressed interferon alpha-mucin fusion protein.

a-e, n = 0.

 GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 30CC

E. coli expressed interferon alpha-mucin fusion protein.

a-e, n = 0.

- GalNAc Transferase, UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

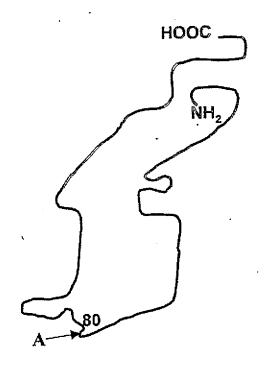
FIG. 30DD

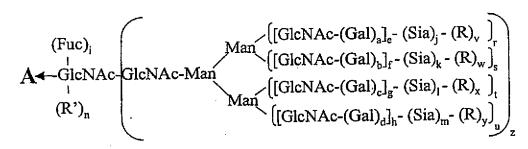
E. coli expressed Interferon alpha (no fusion). a-e, n = 0.

- 1. NHS-CO-linker-SA-CMP
- 2. ST3Gal3, transferrin

a-e=0; n=1; R'=linker-transferrin.

FIG. 30EE





a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = polymer

FIG. 31A

```
CHO, BHK, 293 cells, Vero expressed IF-beta h = 1 to 3; a-g, j-m, i (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; n, v-y = 0; z = 1.
```

1. Sialidase

2. CMP-SA-PEG, ST3Gal3

```
h = 1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.
```

FIG. 31B

```
Insect cell expressed IF-beta
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0 or 1;
z = 1.
```

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 2. CMP-SA-PEG, ST3Gal3, buffer, salt

```
b, d, f, h, k, m, n, s, u, w, y = 0;
a, c, e, g, i, r, t (independently selected) = 0 or 1;
j, l, v, x (independently selected) = 0 or 1;
z = 1; R = PEG.
```

FIG. 31C

```
Yeast expressed IF-beta
a-n = 0; z = 1;
r-y (independently selected) = 0 to 1;
R (branched or linear) = Man, oligomannose or polysaccharide.
```

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- 3.. CMP-SA-PEG, ST3Gal3

a-m, r-z=0; n = 1; R' = -Gal-Sia-PEG.

FIG. 31D

```
CHO, BHK, 293 cells, Vero expressed IF-beta h = 1 to 3; a-g, j-m, i (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; n, v-y = 0; z = 1.
```

1. CMP-SA-PEG, ST3Gal3

```
h = 1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.
```

FIG. 31E

Insect cell expressed IF-beta a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0 or 1; z = 1.

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.

FIG. 31F

Yeast expressed IF-beta a-n = 0; z = 1; r-y (independently selected) = 0 to 1; R (branched or linear) = Man, oligomannose.

- 1. mannosidases
- 2. GNT's 1,2,4,5, UDP-GlcNAc
- 3. Galactosyltransferase, UDP-Gal
- 4.. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z=1; n=0; R=PEG.

FIG. 31G

```
NSO expressed IF-beta
a-i, r-u (independently selected) = 0 or 1;
j-m, n, v-y = 0; z = 1.
```

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 2. H₄N₂-PEG

a-i, j-m, r-y (independently selected) = 0 or 1; n = 0; z = 1; R = PEG.

FIG. 31H

```
CHO, BHK, 293 cells, Vero expressed IF-beta h = 1 to 3; a-g, j-m, i (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; n, v-y = 0; z = 1.
```

1. CMP-SA-PEG, α2,8-ST

```
h = 1 to 3;
a-g, i, r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
z = 1; n = 0; R = PEG.
```

FIG. 311

CHO, BHK, 293 cells, Vero expressed IF-beta a-g, j-m, r-u (independently selected) = 0 or 1; h = 1 to 3; n, v-y = 0; z = 1.

- 1. Sialidase
- 2. Trans-sialidase, PEG-Sia-lactose

a-g, j-m, r-y (independently selected) = 0 or 1; h = 1 to 3; n = 0; z = 1; R = PEG.

FIG. 31J

CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n, v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n=0; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 31K

```
NSO expressed Ifn-beta.

a-d, i-m, r-u, z (independently selected) = 0 or 1;

e-h = 1; n, v-y = 0;

Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α -galactosidase
- 2. α-Galactosyltransferase, UDP-Gal

```
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; R = PEG
n = 0; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
```

FIG. 31L

```
CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n, v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n = 0;
v-y (independently selected) = 0 or 1; R = PEG.
```

FIG. 31M

CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n, v-y=0.

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H₄N₂-PEG

a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n = 0; v-y (independently selected) = 0 or 1; R = PEG.

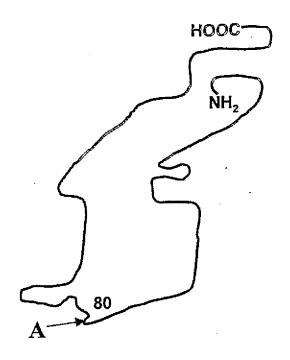
FIG. 31N

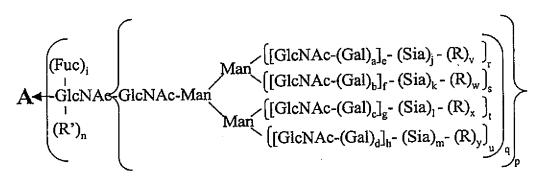
CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n, v-y=0.

1. CMP-SA, α2,8-ST

a-d, i, r-u, z (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; n, v-y (independently selected) = 0.

FIG. 310





a-d, i, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group; R' = H, glycosyl group, modifying group, glycoconjugate.

FIG. 31P

```
Insect cell expressed Ifn-beta.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 31Q

```
Yeast expressed Ifn-beta.

a-m = 0; q-y (independently selected) = 0 to 1;

p = 1;

R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0;
n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.
```

FIG. 31R

CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal3, desialylated transferrin.
- 3. CMP-SA, ST3Gal3

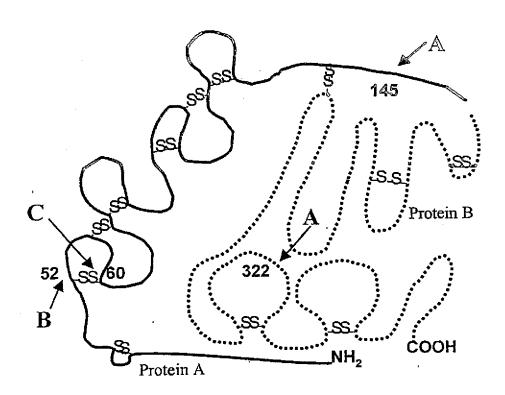
```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-transferrin.
```

FIG. 31S



$$A \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & \operatorname{Man} \left[(\operatorname{GlcNAc-(Gal)}_{a})_{e} - (\operatorname{Sia})_{j} - (\operatorname{R})_{v} \right]_{r} \\ (\operatorname{GlcNAc-GlcNAc-Man} & \left[(\operatorname{GlcNAc-(Gal)}_{b})_{f} - (\operatorname{Sia})_{k} - (\operatorname{R})_{w} \right]_{s} \\ (\operatorname{GlcNAc-(Gal)}_{c})_{g} - (\operatorname{Sia})_{l} - (\operatorname{R})_{x} \right]_{t} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \right]_{u} = 0$$

$$\mathbf{B} \leftarrow \left\{ \text{Gic-}(Xyl)_n \right\}_0$$
 $\mathbf{C} \leftarrow \left\{ \text{Fuc} \right\}_p$

a-d, i, q-u (independently selected) = 0 or 1. o, p (independently selected) = 0 or 1. e-h, n (independently selected) = 0 to 6. j-m (independently selected) = 0 to 20. v-y=0; R = modifying group, mannose, oligomannose, Sia-Lewis X, Sia-Lewis A..

FIG. 32A

```
BHK expressed Factor VII or VIIa
a-d, e, i, g, q, j, l, o, p (independently selected) = 0 or 1;
r, t = 1; f, h, k, m, s, u, v-y = 0; n = 0-4.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mole eq), ST3Gal3

```
a-d, e, g, i, q, j, l, o, p (independently selected) = 0 or 1;
r, t = 1; f, h, k, m, s, u, w, y = 0; n = 0-4;
v, x, (independently selected) = 1,
when j, l (respectively, independently selected) is 1;
R = PEG.
```

FIG. 32B

CHO, BHK, 293 cells, Vero expressed Factor VII or VIIa a-d, e, i, g, q, j, l, o, p (independently selected) = 0 or 1; r, t = 1; f, h, k, m, s, u, v-y = 0; n = 0-4.

- 1. Sialidase
- CMP-SA-PEG (1.2 mole eq), ST3Gal3
- 3. CMP-SA (8 mol eq), ST3Gal3

```
a-d, e, g, i, q, j, l, o, p (independently selected) = 0 or 1;
r, t = 1; f, h, k, m, s, u, w, y = 0; n = 0-4;
v or x, (independently selected) = 1,
when j or l, (respectively, independently selected) is 1;
R = PEG.
```

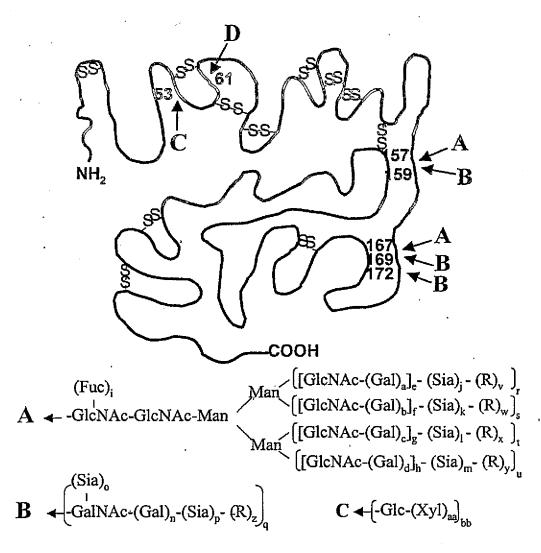
FIG. 32C

```
NSO expressed Factor VII or VIIa
a--u (independently selected) = 0 or 1;
v-y = 0; n = 0-4;
Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α -galactosidase
- 2. Galactosyltransferase, UDP-Gal
- ★ 3. CMP-SA-PEG, ST3Gal3

```
a-m, o-u (independently selected) = 0 or 1;
n = 0-4; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
Sia = Sia; R = PEG.
```

FIG. 32D



$$\mathbf{D} \longleftarrow \text{-Fuc} \Big\{ \text{-} (\text{GlcNAc})_{\text{cc}} \text{-} (\text{Gal})_{\text{dd}} \text{-} (\text{Sia})_{\text{ee}} \Big\}_{\text{ff}} \text{-} (R)_{\text{gg}}$$

a-d, i, n-u (independently selected) = 0 or 1.
bb, cc, dd, ee, ff, gg (independently selected) = 0 or 1.
e-h, aa (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 20.
v-z = 0; R = modifying group, mannose, oligo-mannose.

FIG. 33A

```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected)
= 0 or 1;
o, p, z = 0;
j-m, ee, v-y, gg (independently selected) = 0 or 1;
R = PEG.
```

FIG. 33B

```
CHO, BHK, 293 cells, Vero expressed Factor IX
a-d, n, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, j-m, i, o, p, r-u (independently selected) = 0 or 1;
v-z, gg = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3
- 3. ST3Gal1, CMP-SA

```
a-d, n, p, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, r-u (independently selected) = 0 or 1;
j-m, ee, v-y, gg (independently selected) = 0 or 1;
o, z = 0; R = PEG.
```

FIG. 33C

CHO, BHK, 293 cells, Vero expressed Factor IX a-d, n, q, bb, cc, dd, ff = 1; e-h, aa = 1 to 4; ee, j-m, i, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.

- 1. sialidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA, ST3Gal3
- 4. CMP-SA-PEG, ST3Gal1

```
a-d, n, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, r-u (independently selected) =
0 or 1; R = PEG;
o, v-y, gg = 0;
j-m, p, ee (independently selected) = 0 or 1, but when
p = 1, z = 1.
```

FIG. 33D

```
CHO, BHK, 293 cells, Vero expressed Factor IX
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1;
v-z, gg = 0.
```

CMP-SA-PEG, ST3Gal3

```
a-d, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected)
= 0 or 1; R = PEG;
o, p, z = 0; j-m, ee, v-y, gg (independently selected) =
0 or 1.
```

FIG. 33E

```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H₄N₂-PEG

a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected) = 0 or 1; o, p, z = 0; R = PEG; j-m, ee, v-y, gg (independently selected) = 0 or 1.

FIG. 33F

```
CHO, BHK, 293 cells, Vero expressed Factor IX
a-d, n, q, bb, cc, dd, ff = 1;
e-h, aa = 1 to 4;
ee, j-m, i, o, p, r-u (independently selected) = 0 or 1;
v-z, gg = 0.
```

1. CMP-SA-PEG, α 2,8-ST

```
a-d, q = 1; e-h = 1 to 4;

aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected)

= 0 or 1;

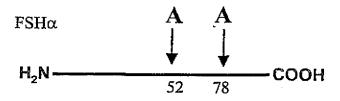
o, p, z = 0; R= PEG;

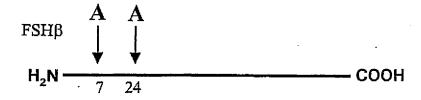
j-m, ee (independently selected) = 0 to 2;

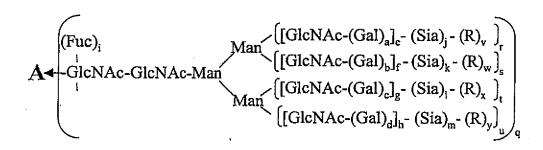
v-y, gg (independently selected) = 1, when j-m

(independently selected) is 2;
```

FIG. 33G







a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose.

FIG. 34A

```
CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 34B

```
CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 34C

```
NSO expressed FSH.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- 2. Galactosyltransferase, UDP-Gal
- ▼ 3. CMP-SA-PEG, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; R = PEG.

FIG. 34D

```
CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 34E

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H₄N₂-PEG

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 34F

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 34G

```
Insect cell expressed FSH.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 34H

```
Yeast expressed FSH.

a-m = 0; q-y (independently selected) = 0 to 1;

p = 1;

R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- ▼ 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0;
n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.
```

FIG. 341

```
CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal1, desialylated chorionic gonadrophin (CG) produced in CHO.
- 3. CMP-SA, ST3Gal3, ST3Gal1

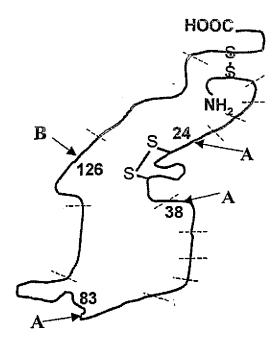
```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-CG.
```

FIG. 34J



$$(Fuc)_{i} \qquad \qquad Man = \begin{bmatrix} [GlcNAc-(Gal)_{a}]_{e} - (Sia)_{j} - (R)_{v} \end{bmatrix}_{r} \\ -GlcNAc-GlcNAc-Man = \begin{bmatrix} [GlcNAc-(Gal)_{b}]_{f} - (Sia)_{k} - (R)_{w} \end{bmatrix}_{s} \\ Man = \begin{bmatrix} [GlcNAc-(Gal)_{b}]_{g} - (Sia)_{l} - (R)_{v} \end{bmatrix}_{t} \\ Man = \begin{bmatrix} [GlcNAc-(Gal)_{c}]_{g} - (Sia)_{l} - (R)_{v} \end{bmatrix}_{t} \\ \begin{bmatrix} [GlcNAc-(Gal)_{d}]_{h} - (Sia)_{m} - (R)_{y} \end{bmatrix}_{u} \\ \end{bmatrix}_{t} \\ B = \begin{bmatrix} (Sia)_{o} \\ -GalNAc-(Gal)_{n} - (Sia)_{p} - (R)_{z} \end{bmatrix}_{q}$$

a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. v-z = 0; R = polymer.

FIG. 35A

```
CHO, BHK, 293 cells, Vero expressed EPO a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; v-z = 0
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-g, n, q = 1; h = 1 to 3;

i, o, p (independently selected) = 0 or 1;

r-u (independently selected) = 0 or 1;

j-m, v-y (independently selected) = 0 or 1;

R = PEG; z = 0.
```

FIG. 35B

```
Insect cell expressed EPO
a-d, f, h, j-q, s, u, v-z = 0;
e, g, i, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 2. CMP-SA-PEG, ST3Gal3

```
b, d, f, h, k, m-q, s, u, w, y, z = 0;
a, c, e, g, i, r, t (independently selected)= 0 or 1;
j, l, v, x (independently selected) = 0 or 1;
R = PEG.
```

FIG. 35C

```
CHO, BHK, 293 cells, Vero expressed EPO a-q, r-u (independently selected) = 0 or 1; v-z = 0.
```

- 1. sialidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA, ST3Gal3
- 4. CMP-SA-PEG, ST3Gall

```
a-h, n, q = 1;
i-m, o, r-u (independently selected) = 0 or 1;
v-y = 0; p, z = 0 or 1; R = PEG.
```

FIG. 35D

```
CHO, BHK, 293 cells, Vero expressed EPO a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; v-z = 0
```

1. CMP-SA-PEG, ST3Gal3

```
a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1;
j-m, v-y (independently selected) = 0 or 1;
R = PEG; z = 0.
```

FIG. 35E

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-q, s, u, v-z=0; e, g, i, r, t (independently selected) = 0 or 1.

- 1. GNT's 1, 2 & 5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

a-c, e-g, i, r-t, v-x (independently selected) = 0 or 1; d, h, j-q, u, y, z = 0; R = PEG.

FIG. 35F

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- 1. GNT's 1, 2 & 5, UDP-GlcNAc
- 2. Galactosidase (synthetic enzyme), PEG-Gal-F.

a-c, e-g, n, q-t, v-x, z (independently selected) = 0 or 1; d, h, j-m, o, p, y, z = 0; R = PEG.

FIG. 35G

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

1. GNT-1, UDP-GlcNAc-PEG

e, i, r, v (independently selected) = 0 or 1; a-h, j-q, s-u, w-z = 0; R = PEG.

FIG. 35H

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- 1. GNT-1, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

a, e, i, r, v (independently selected) = 0 or 1; b-d, f-h, j-q, s-u, w-z = 0; R = PEG.

FIG. 351

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- 1. GNT-1, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 3. ST3Gal3, CMP-SA-PEG

a, e, i, j, r, v (independently selected) = 0 or 1; b-d, f-h, k-q, s-u, w-z = 0; R = PEG.

FIG. 35J

Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- 1. GNT's 1, 2 & 5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 3. ST3Gal3, CMP-SA-PEG

a-c, e-g, i-l, r-t, v-x (independently selected)
= 0 or 1;
d, h, m-q, u, y, z = 0; R = PEG.

FIG. 35K

```
Insect cell, yeast or fungi expressed EPO a-d, f, h, j-m, n-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1, 2 & 5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- ▼ 3. α2,6-sialyltransferase, CMP-SA-PEG

```
a-c, e-g, i-l, r-t, v-x (independently selected)
= 0 or 1;
d, h, m-q, u, y, z = 0; R = PEG.
```

FIG. 35L

```
CHO, BHK, 293 cells, Vero expressed EPO
a-q, r-u (independently selected) = 0 or 1;
v-z = 0.

1. sialidase
2. CMP-SA, ST3Gal3
3. CMP-SA-PEG, ST3Gal1

a-h, q, i-o, r-u (independently selected)
= 0 or 1;
v-y = 0; p, z = 0 or 1; R = PEG.
```

FIG. 35M

CHO, BHK, 293 cells, Vero expressed EPO a-q, r-u (independently selected) = 0 or 1; v-z = 0.

1. CMP-SA-PEG, ST3Gal3

a-h, i-o, q-u (independently selected) = 0 or 1; v-y = 0; p, z = 0 or 1; R = PEG.

FIG. 35N

CHO, BHK, 293 cells, Vero expressed EPO a-q, r-u (independently selected) = 0 or 1; v-z = 0.

1. CMP-SA-PEG, α 2,8-sialyltransferase

a-h, i-o, q-u (independently selected) = 0 or 1; v-y = 0; p, z = 0 or 1; R = SA-PEG.

FIG. 350

CHO, BHK, 293 cells, Vero expressed EPO a-q, r-u (independently selected) = 0 or 1; v-z = 0.

1. CMP-SA-PEG, α2,8-sialyltransferase

a-h, i-o, p-u, v-z (independently selected) = 0 or 1; R = SA-PEG.

FIG. 35P

yeast or fungi expressed EPO
r, t, u, v, x, y (independently selected) = 0 or 1;
a-m, n-q, s, w, z = 0; R = (Man)_n
where n = 1-5, linear or branched.

- 1. mannosidases
- 2. GNT-1, UDP-GlcNAc
- 3. galactosyltransferase, UDP-Gal
- 4. ST3Gal3, CMP-SA-PEG

a, e, j, r, v (independently selected) = 0 or 1; b-d, f-i, k-q, s-u, w-z = 0; R = PEG.

FIG. 35Q

```
yeast or fungi expressed EPO
r, t, u, v, x, y (independently selected) = 0 or 1;
a-m, n-q, s, w, z = 0; R = (Man)<sub>n</sub>
where n = 1-5, linear or branched.
```

- 1. mannosidases
- 2. GNT-1, UDP-GlcNAc-PEG

e, r, v (independently selected) = 0 or 1; a-h, i-q, s-u, w-z = 0; R = PEG.

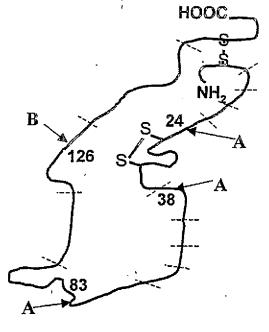
FIG. 35R

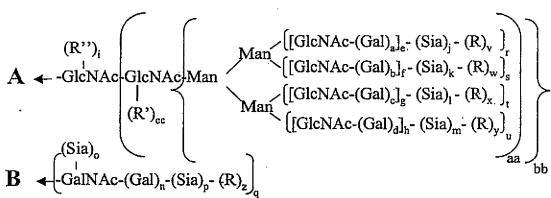
yeast or fungi expressed EPO r, t, u, v, x, y (independently selected) = 0 or 1; a-m, n-q, s, w, z = 0; $R = (Man)_n$ where n = 1-5, linear or branched.

- 1. mannosidase-I
- 2. GNT-1, UDP-GlcNAc
- 3. galactosyltransferase, UDP-Gal
- 4. ST3Gal3, CMP-SA-PEG

```
a, e, j, r, t-u, v, x, y (independently selected)
= 0 or 1;
b-d, f-i, k-q, s, w, z = 0;
(R)<sub>v</sub> = PEG; (R)<sub>x</sub> and (R)<sub>y</sub> = Man.
```

FIG. 35S





a-d, i, n-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 to 20.

v-z=0; aa, bb=1; cc=0;

R = polymer; R'' and R' = sugar-polymer or Fuc.

FIG. 35T

```
yeast or fungi expressed EPO
r, t, u, v, x, y (independently selected) = 0 or 1;
cc, a-m, n-q, s, w, z = 0;
aa, bb = 1;
R = (Man), where n = 1-100, linear or branched.
```

- 1. endo-H
- 2. galactosyltransferase, UDP-Gal-PEG

```
i (independently selected) = 0 or 1;
aa, bb, cc, a-h, j-z = 0; R" = Gal-PEG.
```

FIG. 35U

```
yeast or fungi expressed EPO
r, t, u, v, x, y (independently selected) = 0 or 1;
cc, a-m, n-q, s, w, z = 0; aa, bb = 1;
R = (Man)<sub>n</sub> where n = 1-100, linear or branched.
```

- 1. endo-H
- 2. galactosyltransferase, UDP-Gal
- 3. ST3Gal3, CMP-SA-PEG

```
i (independently selected) = 0 or 1;
aa, bb, cc, a-h, j-z = 0; R" = Gal-SA-PEG.
```

FIG. 35V

```
Insect cell expressed EPO

a-d, f, h, j-m, n-q, s, u, v-z = 0;

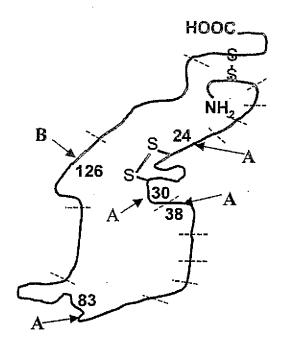
e, g, i, r, t (independently selected) = 0 or 1;

aa = 1; R" = Fuc.
```

- 1. mannosidases
- 2. galactosyltransferase, UDP-Gal-PEG

```
cc, e, i, r, v (independently selected) = 0 or 1;
bb, a-h, j-q, s-u, w-z = 0; aa = 1; R' = Gal-PEG.
```

FIG. 35W



$$(Fuc)_{i}$$

$$A \leftarrow -GlcNAc-GlcNAc-Man$$

$$= -GlcNAc-GlcNAc-GlcNAc-GlcNac-Gll)t - (Sia)t - (Sia$$

FIG. 35X

```
NSO expressed NESP
q = 1; a-i, n, r-u (independently selected) = 0
or 1; j-m, o, p, v-z = 0
```

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H_aN₂-PEG

q = 1; a-i, j-n, r-y (independently selected) = 0 or 1;
o, p, z = 0; R = PEG.

FIG. 35Y

```
CHO, BHK, 293 cells, Vero expressed NESP a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; v-z = 0
```

1. CMP-SA-PEG, α 2,8-ST

```
a-g, n, q = 1; h = 1 to 3;

i, o, p (independently selected) = 0 or 1;

r-u (independently selected) = 0 to 1;

j-m (independently selected) = 0 to 2;

v-y (independently selected) = 1,

when j-m (independently selected) is 2;

R = PEG; z = 0.
```

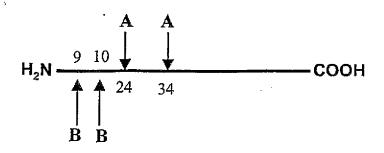
FIG. 35Z

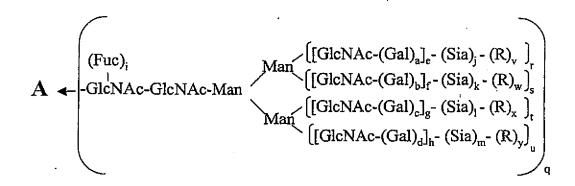
CHO, BHK, 293 cells, Vero expressed NESP a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; v-z = 0

1 CMP-SA, poly- α 2,8-ST

a-g, n, q = 1; h = 1 to 3; i, j-m, o, p, r-u, (independently selected) = 0 or 1; v-z (independently selected) = 0-40; R = Sia.

FIG. 35AA





$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{Sia})_{o} \\ -\operatorname{GalNAc-(Gal)}_{n} - (\operatorname{Sia})_{p} - (R)_{z} \end{pmatrix}_{aa}$$

a-d, i, n-u, aa (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer, glycoconjugate.

FIG. 36A

CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u, aa (independently selected) = 0 or 1;
o, p, z = 0; n, e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 36B

CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3 & ST3Gal1

a-d, i-m, p-u, aa (independently selected) = 0 or 1; o, z = 0; n, e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 36C

```
NSO expressed GM-CSF.
a-d, i-m, o-u, aa (independently selected) = 0 or 1;
n, e-h = 1; v-z = 0;
Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- 2. CMP-SA, ST3Gal3
- 2. CMP-SA-PEG, ST3Gal1

a-d, i-m, p-u, z, aa (independently selected) = 0 or 1; n, e-h = 1; o, v-y = 0; z = 1, when p = 1; R = PEG.

FIG. 36D

```
CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

a-d, i-m, q-y, as (independently selected) = 0 or 1; o, p, z = 0; n, e-h = 1; R = PEG.

FIG. 36E

CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h=1; v-z=0.

- 1. CMP-SA-levulinate, ST3Gal3, buffer, salt
- 2. H₄N₂-PEG

a-d, i-m, o-y, aa (independently selected) = 0 or 1; z = 0; n, e-h = 1; R = PEG.

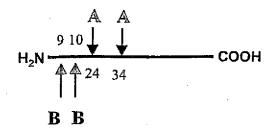
FIG. 36F

CHO, BHK, 293 cells, Vero expressed GMCSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h=1; v-z=0.

1. CMP-SA, α2,8-ST

a-d, i, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; j-m (independently selected) = 0-20; v-z (independently selected) = 0.

FIG. 36G



$$A \leftarrow \begin{array}{c} \\ \text{(Fuc)}_{i} \\ \text{GlcNAc-(Gal)}_{a}]_{e} - (\text{Sia)}_{j} - (\text{R)}_{v} \\ \text{[GlcNAc-(Gal)}_{b}]_{f} - (\text{Sia)}_{k} - (\text{R)}_{w} \\ \text{[GlcNAc-(Gal)}_{c}]_{g} - (\text{Sia)}_{1} - (\text{R)}_{x} \\ \text{(R')}_{cc} \\ \end{array}$$

$$\begin{array}{c} \text{(GlcNAc-(Gal)}_{b}]_{f} - (\text{Sia)}_{g} - (\text{Sia)}_{1} - (\text{R)}_{x} \\ \text{[GlcNAc-(Gal)}_{d}]_{h} - (\text{Sia)}_{m} - (\text{R)}_{y} \\ \text{(b)} \\ \end{array}$$

$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{0} \\ -\mathrm{GalNAc} \cdot (\mathrm{Gal})_{n} \cdot (\mathrm{Sia})_{p} \cdot (\mathrm{R})_{z} \end{bmatrix}_{\mathrm{aa}}$$

a-d, i, n-u, aa, bb, cc (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0; R = modifying group, mannose, oligo-mannose.
R'= H, glycosyl residue, modifying group. glycoconjugate.

FIG. 36H

```
Insect cell expressed GM-CSF.
a-d, f, h, j-m, o, p, s, u, v-z = 0;
e, g, i, n, q, r, t, aa (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, n, q-u (independently selected) = 0 or 1;

j-m = 0; v-y (independently selected) = 1,

when e-h (independently selected) is 1;

R = PEG.
```

FIG. 361

```
Yeast expressed GM-CSF.
a-p, z, cc = 0;
q-y, aa (independently selected) = 0 to 1;
bb = 1; R (branched or linear) = Man, oligomannose;
GalNAc = Man.
```

- 1. Endoglycanase
- 2. mannosidase (if aa = 1).
- 3. Galactosyltransferase, UDP-Gal-PEG

```
a-p, r-z, aa, bb = 0;
q, cc (independently selected) = 0 or 1;
R' = -Gal-PEG.
```

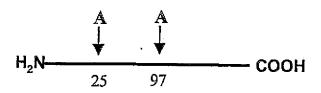
FIG. 36J

CHO, BHK, 293 cells, Vero expressed GM-CSF. a-m, o-u, aa, bb (independently selected) = 0 or 1; n, v-z, cc = 0.

- 1. sialidase
- 2. CMP-SA, ST3Gal3
- 2. CMP-SA-linker-SA-CMP, ST3Gal1
- 3. ST3Gal3, transferrin

a--m, p-u, z, as (independently selected) = 0 or 1; o, v-y, cc = 0; bb, n = 1; R = transferrin.

FIG. 36K



$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e^{-}} \left(\operatorname{Sia} \right)_{j} - \left(\operatorname{R} \right)_{v} \end{bmatrix}_{r} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f^{-}} \left(\operatorname{Sia} \right)_{k} - \left(\operatorname{R} \right)_{w} \right]_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{c} \right]_{g^{-}} \left(\operatorname{Sia} \right)_{l} - \left(\operatorname{R} \right)_{x} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \end{bmatrix}_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{t} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{u} \right]_{t} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{u} \right]_{t} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{u} \right]_{t} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{u} \right]_{t} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{u} \right]_{t} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{u} \right]_{t} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{u} \right]_{t} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{Sia} \right)_{u} \right]_{t} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia} \right)_{u} \right]_{t} \\ \left[\operatorname{GlcNAc-$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 37A

```
CHO, BHK, 293 cells, Vero expressed IF-gamma. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 37B

```
CHO, BHK, 293 cells, Vero expressed IF-gamma. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 37C

```
NSO expressed Interferon gamma.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- 2. α-Galactosyltransferase, UDP-Gal

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 37D

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 37E

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

```
1. CMP-SA-levulinate, ST3Ga13,
```

2. H_4N_2 -PEG

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

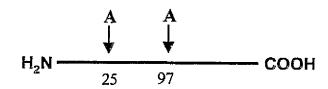
FIG. 37F

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

1. CMP-SA, α2,8-ST

```
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-20;
v-y (independently selected) = 0.
```

FIG. 37G



$$A = (\operatorname{Fuc})_{i} \\ \operatorname{GlcNAc-\operatorname{Gal})_{a}}_{e} - (\operatorname{Sia})_{j} - (\operatorname{R})_{v} \\ \operatorname{GlcNAc-\operatorname{Gal})_{b}}_{r} - (\operatorname{Sia})_{k} - (\operatorname{R})_{w} \\ \operatorname{GlcNAc-\operatorname{Gal})_{b}}_{r} - (\operatorname{Sia})_{k} - (\operatorname{R})_{w} \\ \operatorname{GlcNAc-\operatorname{Gal})_{c}}_{g} - (\operatorname{Sia})_{l} - (\operatorname{R})_{x} \\ \operatorname{[GlcNAc-\operatorname{Gal})_{d}}_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \\ \operatorname{[GlcNAc-\operatorname{Gal})_{d}}_{p} - (\operatorname{Sia})_{m} - (\operatorname{R})_{m} - (\operatorname{R})_{m} - (\operatorname{R})_{m} \\ \operatorname{[GlcNAc-\operatorname{Gal})_{d}}_{p} - (\operatorname{Sia})_{m} - (\operatorname{R})_{m} - (\operatorname{R})_{m} - (\operatorname{R})_{m} \\ \operatorname{[GlcNAc-\operatorname{Gal})_{d}}_{p} - (\operatorname{Sia})_{m} - (\operatorname{R})_{m} - (\operatorname{R})_{m}$$

a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 37H

```
Insect or fungi cell expressed IF-gamma.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 371

```
Yeast expressed IF-gamma.

a-m = 0; q-y (independently selected) = 0 to 1; p = 1;

R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.
```

FIG. 37J

```
CHO, BHK, 293 cells, Vero expressed IF-gamma. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, transferrin treated with endoglycanase.

```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-transferrin.
```

FIG. 37K

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h, p = 1; n, v-y = 0.
```

1. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h, p = 1;
n, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 37L

```
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT's 1 & 2, UDP-GlcNAc-PEG

a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, q (independently selected) = 0 or 1;
p = 1; v, x (independently selected) = 1,
when e, g (independently selected) is 1;
R = PEG.
```

Insect or fungi cell expressed IF-gamma.

FIG. 37M

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

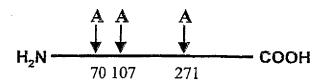
1. CMP-SA-PEG, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-2;
v-y (independently selected) = 1,
```

when j-m (independently selected) = 2;

FIG. 37N

R = PEG.



$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & \operatorname{Man} & \left[(\operatorname{GlcNAc-(Gal)}_{a})_{e^{-}} & (\operatorname{Sia})_{j} - (\operatorname{R})_{v} \right]_{r} \\ (\operatorname{GlcNAc-GlcNAc-Man} & \left[(\operatorname{GlcNAc-(Gal)}_{b})_{f^{-}} & (\operatorname{Sia})_{k} - (\operatorname{R})_{w} \right]_{s} \\ \operatorname{Man} & \left[(\operatorname{GlcNAc-(Gal)}_{c})_{g^{-}} & (\operatorname{Sia})_{l} - (\operatorname{R})_{x} \right]_{t} \\ \left[(\operatorname{GlcNAc-(Gal)}_{d})_{h^{-}} & (\operatorname{Sia})_{m^{-}} & (\operatorname{R})_{y} \right]_{u} \\ \operatorname{GlcNAc-(Gal)}_{d} & \operatorname{Cond}_{d} & \operatorname{Cond$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 38A

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed α<sub>1</sub> antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 38B

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed α<sub>1</sub> antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

- 1. Sialidase
- CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 38C

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed alpha-1 antitrypsin.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3GaI3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 38D

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed α<sub>1</sub>-antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

```
    CMP-SA-levulinate, ST3Gal3,
buffer, salt
    2. H<sub>4</sub>N<sub>2</sub>-PEG
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

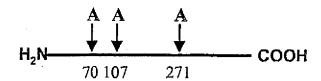
FIG. 38E

CHO, BHK, 293 cells, Vero expressed α_1 -antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 38F



$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & & & \\ (\operatorname{Fuc})_{i} & & & \\ (\operatorname{GlcNAc-(Gal)}_{a})_{e^{-}} (\operatorname{Sia})_{j} - (\operatorname{R})_{v} \\ (\operatorname{GlcNAc-(Gal)}_{b})_{f^{-}} (\operatorname{Sia})_{k} - (\operatorname{R})_{w} \\ (\operatorname{GlcNAc-(Gal)}_{c})_{g^{-}} (\operatorname{Sia})_{l} - (\operatorname{R})_{x} \\ (\operatorname{R}')_{n} & & & \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h^{-}} (\operatorname{Sia})_{m^{-}} (\operatorname{R})_{y} \end{bmatrix}_{u} \\ q_{p}$$

a-d, i, n, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 38G

```
Insect or fungi cell expressed \alpha_1-antitrypsin.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1; j-m = 0;
v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 38H

```
Yeast expressed \alpha_1-antitrypsin.

a-m=0; q-y (independently selected) = 0 to 1;

p=1; R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

FIG. 381

CHO, BHK, 293 cells, Vero expressed α_1 -antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

- 1. CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, transferrin treated with endoglycanase

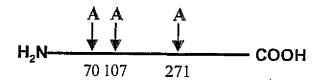
```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-transferrin.
```

FIG. 38J



$$(Fuc)_{i}$$

$$A \leftarrow GlcNAc-Man$$

$$(R')_{p}$$

$$(R')_{q}$$

$$(GlcNAc-(Gal)_{a}]_{e} - (Sia)_{j} - (R)_{v}$$

$$[GlcNAc-(Gal)_{b}]_{f} - (Sia)_{k} - (R)_{w}$$

$$[GlcNAc-(Gal)_{c}]_{g} - (Sia)_{l} - (R)_{x}$$

$$[GlcNAc-(Gal)_{d}]_{h} - (Sia)_{m} - (R)_{y}$$

$$[GlcNAc-(Gal)_{d}]_{h} - (Sia)_{m} - (R)_{y}$$

a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. R = polymer; R', R" (independently selected) = sugar, glycoconjugate.

FIG. 38K

Yeast expressed alpha-1 antitrypsin.
a-h, i-m, p, q = 0;
R (independently selected) = mannose, oligomannose, polymannose;
r-u, v-y (independently selected) = 0 or 1; n, o = 1.

- 1. endoglycanase

a-h, i-o, q, r-u, v-y = 0; p = 1. R" = Gal-PEG.

FIG. 38L

Plant expressed alpha-1 antitrypsin. a-d, f, h, j-m, s, u, v-y = 0; e, g, i, q, r, t (independently selected) = 0 or 1; n=1; R' = xylose

- 1. hexosaminidase,
- 2. alpha mannosidase and xylosidase
- 3. GlcNAc transferase, UDP-GlcNAc-PEG

a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0; q = 1; R' = GlcNAc-PEG.

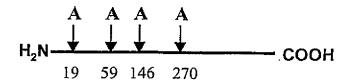
FIG. 38M

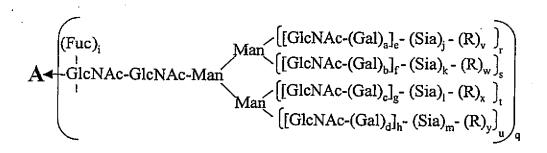
CHO, BHK, 293 cells, Vero, transgenic animal expressed α₁ antitrypsin.
a-h, i-o, r-u (independently selected) = 0 or 1;
p, q, v-y = 0.

1. CMP-SA-PEG, ST3Gal3

a-h, i-o, r-u (independently selected) = 0 or 1; p, q = 0; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 38N





a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 39A

```
CHO, BHK, 293 cells, Vero expressed Cerezyme a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 39B

```
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-M-6-P (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = mannose-6-phosphate
```

FIG. 39C

```
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = Mannose-6-phosphate
```

FIG. 39D

```
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. CMP-SA-levulinate, ST3Gal3, buffer, salt
- 2. H₄N₂-spacer-M-6-P or clustered M-6-P

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = M-6-P or clustered M-6-P
```

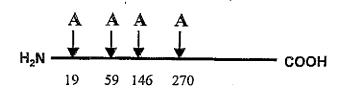
FIG. 39E

CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 39F



$$A \leftarrow \begin{array}{c} \\ \text{(Fuc)}_{i} \\ \text{GlcNAc-Man} \\ \text{(GlcNAc-(Gal)}_{a}]_{e} - (Sia)_{j} - (R)_{v} \\ \text{[GlcNAc-(Gal)}_{b}]_{f} - (Sia)_{k} - (R)_{w} \\ \text{[GlcNAc-(Gal)}_{c}]_{g} - (Sia)_{l} - (R)_{x} \\ \text{(R')}_{n} \\ \text{[GlcNAc-(Gal)}_{d}]_{h} - (Sia)_{m} - (R)_{y} \\ \text{[GlcNAc-(Gal)}_{d}]_{h} - (R$$

a-d, i, n, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 39G

```
Insect cell expressed Cerezyme.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0;
v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 39H

```
Yeast expressed Cerezyme.

a-m = 0; q-y (independently selected) = 0 to 1;

p = 1; R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal

a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

FIG. 391

```
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

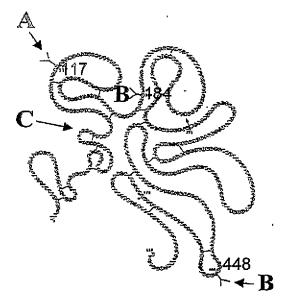
- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal3, desialylated transferrin.
- 3. CMP-SA, ST3Gal3

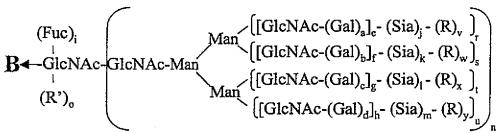
```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0; v-y (independently selected) = 0 or 1;

R = linker-transferrin.
```

FIG. 39J





$$\mathbf{C} \leftarrow \text{-(Fuc)}_{0-1}$$
 $\mathbf{A} \leftarrow \text{-GlcNAc-GlcNAc-Man}$
 $\mathbf{Man} - [\text{Man}]_{0-12}$
 $[\text{Man}]_{0-6}$
 $[\text{Man}]_{0-6}$

a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. R = polymer; R' = sugar, glycoconjugate.

FIG. 40A

```
CHO, BHK, 293 cells, Vero expressed tPA a-g, n = 1; h = 1 to 3; j-m, i, (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; o, v-y = 0.
```

- 1. Mannosidase(s), sialidase
- 2. GNT1,2 (4 and/or 5) UDP-GlcNAc
- 3. Gal transferase, UDP-Gal
- 4. CMP-SA-PEG, ST3Gal3

```
A = B; a-g, n = 1; h = 1 to 3;
i, r-u (independently selected) = 0 or 1;
o = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG
```

FIG. 40B

```
Insect or fungi cell expressed tPA A = B; a-d, f, h, j-o, s, u, v-y = 0; e, g, i, n, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- **★** 3. CMP-SA-PEG, ST3Gal3

```
A = B; b, d, f, h, k, m, o, s, u, w, y = 0;
a, c, e, g, i, r, t (independently selected) = 0 or 1;
n = 1; j, l, v, x (independently selected) = 0 or 1;
R = PEG.
```

FIG. 40C

Yeast expressed tPA B = A; i = 0.

- 1. endoglycanase
- 2. Galactosyltransferase, UDP-Gal-PEG

A = B; a-n, r-y = 0; o = 1; R' = Gal-PEG.

FIG. 40D

Insect or fungi cell expressed tPA A = B; a-d, f, h, j-o, s, u, v-y = 0; e, g, i, n, r, t (independently selected) = 0 or 1.

- 1. alpha and beta mannosidases
- 2. Galactosyltransferase, UDP-Gal-PEG

A = B; a-n, r-y = 0; o = 1; R' = Gal-PEG.

FIG. 40E

```
Insect or fungi cell expressed tPA

A = B; a-d, f, h, j-o, s, u, v-y = 0;
e, g, i, n, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
A = B; b, d, f, h, j-o, s, u, w, y = 0;
a, c, e, g, i, r, t, v, x (independently selected)= 0 or 1;
n = 1; R = PEG.
```

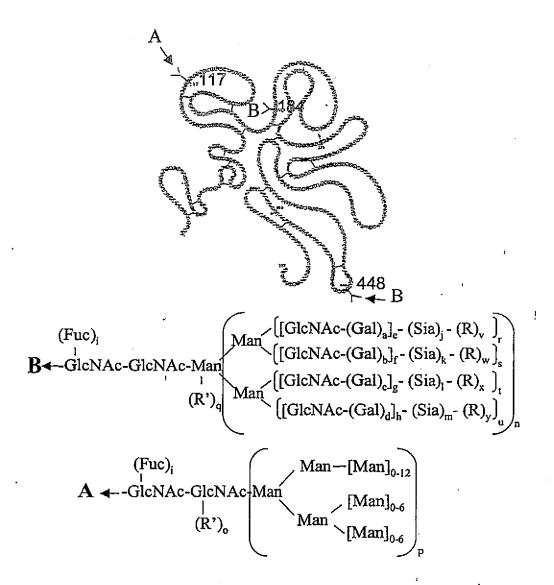
FIG. 40F

```
Insect or fungi cell expressed tPA
A = B; a-d, f, h, j-o, s, u, v-y = 0;
e, g, i, n, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1 & 2, UDP-GlcNAc
- 2. Galactosidase (synthetic enzyme), PEG-Gal-F.

```
A = B; b, d, f, h, j-o, s, u, w, y = 0;
a, c, e, g, i, r, t, v, x (independently selected)= 0 or 1;
n = 1; R = PEG.
```

FIG. 40G



a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. R = polymer; R' = sugar, glycoconjugate.

FIG. 40H

```
NSO expressed tPA
A = B; a-m, r-u (independently selected) = 0 or 1;
n = 1; o, p, q, v-y = 0
```

- 1. sialidase, alpha-galactosidase
- 2. CMP-SA-levulinate, ST3Gal3,
- 3. H₄N₂-PEG

```
A = B; a-m, r-y (independently selected) = 0 or 1;

n = 1; o, p, q = 0;

v-y (independently selected) = 1,

when j-m (independently selected) is 1;

R = PEG.
```

FIG. 401

```
CHO, BHK, 293 cells, Vero expressed tPA a-g, n, p = 1; h = 1 to 3; j-m, i, (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; q, o, v-y = 0.
```

- 1. alpha and beta Mannosidases
- 2. CMP-SA, ST3Gal3
- 3. Galactosyltransferase, UDP-Gal-PEG

```
a-g, n = 1; h = 1 to 3;
i, r-u (independently selected) = 0 or 1; o = 1;
q, p, v-y = 0; j-m (independently selected) = 0 or 1;
R' = Gal-PEG
```

FIG. 40J

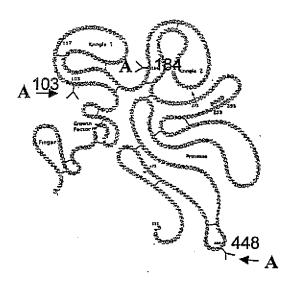
```
Plant expressed tPA

A = B; a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1;
n = 1; R' = xylose
```

- 1. hexosaminidase,
- 2. alpha mannosidase and xylosidase
- 3. GlcNAc transferase, UDP-GlcNAc-PEG

```
A = B; a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0;
q = 1; R' = GlcNAc-PEG.
```

FIG. 40K



$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e^{-}} \left(\operatorname{Sia} \right)_{j^{-}} \left(\operatorname{Rl}_{v} \right)_{r} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f^{-}} \left(\operatorname{Sia} \right)_{k^{-}} \left(\operatorname{Rl}_{w} \right)_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{g^{-}} \left(\operatorname{Sia} \right)_{t^{-}} \left(\operatorname{Rl}_{v} \right)_{t^{-}} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{Rl}_{v} \right)_{y} \right]_{u} \\ q = \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{Rl}_{v} \right)_{y} \right]_{u} \\ q = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{Rl}_{v} \right)_{y} \\ q = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{Rl}_{v} \right)_{y} \\ q = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{Rl}_{v} \right)_{y} \\ q = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{Rl}_{v} \right)_{y} \\ q = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{Rl}_{v} \right)_{y} \\ q = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{Rl}_{v} \right)_{y} \\ q = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{y} \\ q = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{y} \\ q = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{y} \\ q = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{y} \\ q = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{y} \\ q = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \right]_{y} \\ q = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \\ q = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 40L

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 40M

```
CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 40N

```
NSO expressed TNK tPA

a-d, i-m, q-u (independently selected) = 0 or 1;

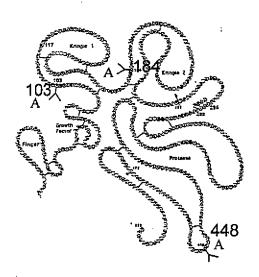
e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- 2. Galactosyltransferase, UDP-Gal

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 400



$$\mathbf{A} \leftarrow \begin{bmatrix} \left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e^{-}} \left(\operatorname{Sia} \right)_{j} - \left(\operatorname{R} \right)_{v} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f^{-}} \left(\operatorname{Sia} \right)_{k} - \left(\operatorname{R} \right)_{w} \right]_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{c} \right]_{g^{-}} \left(\operatorname{Sia} \right)_{l} - \left(\operatorname{R} \right)_{x} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u} \right]_{q} \\ = \underbrace{\left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u}}_{q} \left[\underbrace{\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia} \right)_{m^{-}} \left(\operatorname{R} \right)_{y} \right]_{u}}_{q} \right]_{q}}_{q}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 40P

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 40Q

```
CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

```
    CMP-SA-levulinate, ST3Gal3,
buffer, salt
    H<sub>4</sub>N<sub>2</sub>-PEG
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

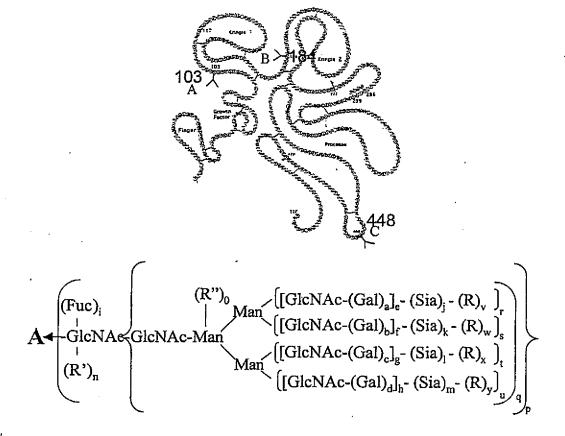
FIG. 40R

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 40S



a-d, i, n-y (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 100.

R = modifying group, mannose, oligo-mannose;

R' = H, glycosyl residue, modifying group, glycoconjugate.

R" = glycosyl residue.

FIG. 40T

```
Insect cell expressed TNK tPA
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;

j-m = 0; v-y (independently selected) = 1,

when e-h (independently selected) is 1;

R = PEG.
```

FIG. 40U

```
Yeast expressed TNK tPA
a-m = 0; q-y (independently selected) = 0 to 1; p = 1;
R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-PEG.
```

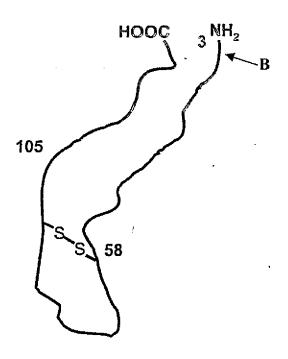
FIG. 40V

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, anti-TNF IG chimera produced in CHO.

a-m, r-u (independently selected) = 0 or 1; p, q = 1; n = 0; v-y (independently selected) = 0 or 1; R = linker-anti-TNF IG chimera protein.

FIG. 40W



$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc-(Gal)_{a}-(Sia)_{c}-(R)_{d}} \end{bmatrix}_{c}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = modifying group, mannose, oligomannose.

FIG. 41A

CHO, BHK, 293 cells, Vero expressed IL-2 a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 41B

Insect cell expressed IL-2 a, e (independently selected) = 0 or 1; b, c, d = 0.

- 1. Galactosyltransferase, UDP-Gal
- 2. CMP-SA-PEG, ST3Gal1

a, c, d, e (independently selected) = 0 or 1; R = PEG.

FIG. 41C

```
E. coli expressed IL-2
a-e = 0.

1. GalNAc Transferase, UDP-GalNAc
2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1;
a, b = 0; R = PEG.
```

FIG. 41D

```
NSO expressed IL-2
a, e (independently selected) = 0 or 1;
b, c, d = 0

1. CMP-SA-levulinate, ST3Gal1
2. H_4N_2-PEG

a, c, d, e (independently selected) = 0 or 1;
b = 0; R = PEG.
```

FIG. 41E

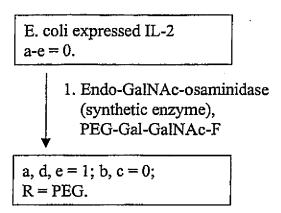


FIG. 41F

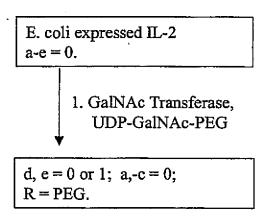


FIG. 41G

2 peptides

A and A' - N-linked sites

 ${f B}$ - O-linked sites

$$(Fuc)_{i} \qquad ([GlcNAc-(Gal)_{a}]_{e}-(Sia)_{j}-(R)_{v})_{r}$$

$$([GlcNAc-(Gal)_{b}]_{f}-(Sia)_{k}-(R)_{w})_{s}$$

$$([GlcNAc-(Gal)_{c}]_{g}-(Sia)_{l}-(R)_{x})_{t}$$

$$([GlcNAc-(Gal)_{d}]_{h}-(Sia)_{m}-(R)_{y})_{u}$$

$$([GlcNAc-(Gal)_{d}]_{h}-(Sia)_{m}-(R)_{y})_{u}$$

$$([GlcNAc-(Gal)_{d}]_{h}-(Sia)_{m}-(R)_{y})_{u}$$

$$\mathbf{B} \quad \bullet \begin{array}{c} \text{(Sia)}_{o} \\ \text{-GalNAc-(Gal)}_{n}\text{-(Sia)}_{p}\text{- (R)}_{z} \end{array} \right]_{q}$$

a-d, i, n-u (independently selected) = 0 or 1. aa, bb (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 20. v-z=0; R = polymer, glycoconjugate.

FIG. 42A

CHO, BHK, 293s cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, a-d, j-m, i, n-u (independently selected) = 0 or 1;

v-z = 0.

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

e-h = 1 to 4; aa, bb, a-d, i, n, q-u (independently selected) = 0 or 1; o, p, z = 0; j-m, v-y (independently selected) = 0 or 1; R = PEG.

FIG. 42B

CHO, BHK, 293S cells, Vero, MDCK, 293S, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, a-d, j-m, i, n-u (independently selected) = 0 or 1;

v-z = 0.

- 1. Sialidase
 - 2. CMP-SA-PEG, ST3Gal3
 - 3. ST3Gal1, CMP-SA

e-h = 1 to 4; aa, bb, a-d, i, n, p-u (independently selected) = 0 or 1; o, z = 0; j-m, v-y (independently selected) = 0 or 1; R = PEG.

FIG. 42C

```
CHO, BHK, 293s cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, a-d, j-m, i, n-u (independently selected)=0 or 1;

v-z = 0.
```

1. CMP-SA-PEG, ST3Gal3

```
e-h = 1 to 4;
aa, bb, a-d, i, n-u (independently selected) = 0 or 1;
z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 42D

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, a-d, j-m, i, n-u (independently selected) 0 or 1;

v-z = 0.
```

1. CMP-SA-PEG, ST3Gal1

```
e-h = 1 to 4;
aa, bb, a-d, i, n-u (independently selected) = 0 or 1;
z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 42E

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, a-d, j-m, i, n-u (independently selected)=0 or 1;

v-z = 0.
```

1. CMP-SA-PEG, α2,8-ST

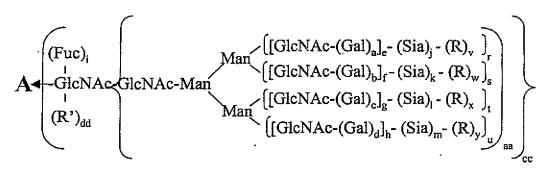
```
e-h = 1 to 4;
aa, bb, a-d, i, n-y (independently selected) = 0 or 1;
z = 0; j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
R = PEG.
```

FIG. 42F

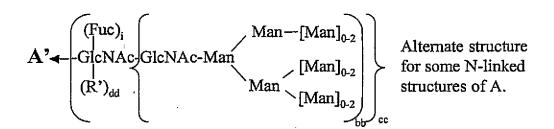
2 peptides

A OF A? - N-linked sites

B - O-linked sites



$$\mathbf{B} = \left(\begin{array}{c} (\mathrm{Sia})_{0} \\ -(\mathrm{GalNAc-(Gal)}_{n} - (\mathrm{Sia})_{p} - (\mathrm{R})_{z} \end{array} \right)_{0}$$



a-d, i, n-u, (independently selected) = 0 or 1.
aa, bb, cc, dd (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 20.
v-z = 0;
R = modifying group, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 42G

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;

dd, v-z = 0.
```

CMP-SA-levulinate, ST3Gal3,
 L₄N₂-PEG

```
e-h = 1 to 4;
aa, bb, cc, a-d, i, n-u (independently selected) = 0 or 1;
dd, z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 42H

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;

dd, v-z = 0.
```

1. endo-H2. galactosyltransferase, UDP-Gal-PEG

```
e-h = 1 to 4;
aa, bb, dd, a-d, i, j-u (independently selected) = 0 or 1;
cc, v-z = 0; R' = -Gal-PEG.
```

FIG. 421

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;

dd, v-z = 0.
```

- 1. ST3Gal3, CMP-SA
- 2. endo-H
- 3. galactosyltransferase, UDP-Gal-PEG

```
e-h = 1 to 4;
aa, bb, dd, a-d, i, j-u (independently selected) = 0 or 1;
cc, v-z = 0; R' = -Gal-PEG.
```

FIG. 42J

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;

dd, v-z = 0.
```

- 1. mannosidases
- 2. GNT 1 & 2, UDP-GlcNAc
- 3. galactosyltransferase, UDP-Gal-PEG

```
e-h = 1 to 4;
aa, a-d, i, j-y (independently selected) = 0 or 1;
bb, cc, dd, z = 0; R = PEG.
```

FIG. 42K

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.
```

- 1. mannosidases
- 2. GNT-1,2, 4 & 5; UDP-GlcNAc
- ★ 3. galactosyltransferase, UDP-Gal
 - 4. ST3Gal3, CMP-SA

```
e-h = 1 to 4;
aa, bb, cc, a-d, i, j-q (independently selected) = 0 or 1;
dd, v-z=0.
```

FIG. 42L

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.

e-h = 1 to 4;

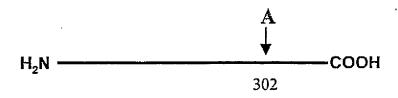
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;

dd, v-z = 0.
```

1. mannosidases
2. GNT-1, ÚDP-GlcNAc-PEG

```
e-h = 0 to 4;
aa, a-d, i, j-y (independently selected) = 0 or 1;
bb, cc, dd, z = 0.
```

FIG. 42M



$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & \operatorname{Man} & \left[(\operatorname{GlcNAc-(Gal)}_{a})_{e^{-}} & (\operatorname{Sia})_{j} - (\operatorname{R})_{v} \right]_{r} \\ (\operatorname{GlcNAc-GlcNAc-Man} & \left[(\operatorname{GlcNAc-(Gal)}_{b})_{f^{-}} & (\operatorname{Sia})_{k} - (\operatorname{R})_{w} \right]_{s} \\ \operatorname{Man} & \left[(\operatorname{GlcNAc-(Gal)}_{c})_{g^{-}} & (\operatorname{Sia})_{i} - (\operatorname{R})_{x} \right]_{t} \\ \left[(\operatorname{GlcNAc-(Gal)}_{d})_{h^{-}} & (\operatorname{Sia})_{m^{-}} & (\operatorname{R})_{y} \right]_{u} \\ \operatorname{GlcNAc-(Gal)}_{d} & \operatorname{GlcNAc-(Gal)}_{d} &$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 43A

CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.

FIG. 43B

CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 43C

```
CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 43D

```
CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- 1. CMP-SA-levulinate, ST3Gal3, buffer, salt
- 2. H₄N₂-PEG

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

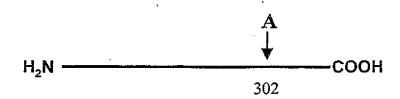
FIG. 43E

```
CHO, BHK, 293 cells, Vero expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

1. CMP-SA, α 2,8-ST

```
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1;
j-m (independently selected) = 0-20;
v-y (independently selected) = 0.
```

FIG. 43F



$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & & & \\ (\operatorname{GlcNAc-(Gal)}_{a}]_{e^{-}} (\operatorname{Sia})_{j^{-}} (\operatorname{R})_{v} \\ (\operatorname{GlcNAc-(Gal)}_{b}]_{f^{-}} (\operatorname{Sia})_{k^{-}} (\operatorname{R})_{w} \end{bmatrix}_{s} \\ (\operatorname{R}')_{n} & & & & & \\ (\operatorname{GlcNAc-(Gal)}_{b}]_{g^{-}} (\operatorname{Sia})_{l^{-}} (\operatorname{R})_{x} \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (\operatorname{R})_{y} \end{bmatrix}_{u} \\ q \\ p \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (\operatorname{R})_{y} \end{bmatrix}_{u} \\ q \\ p \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (\operatorname{R})_{y} \end{bmatrix}_{u} \\ q \\ p \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (\operatorname{R})_{y} \\ q \\ p \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (\operatorname{R})_{y} \\ q \\ p \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (\operatorname{R})_{y} \\ q \\ p \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h^{-}} (\operatorname{Sia})_{m^{-}} (\operatorname{R})_{y} \\ q \\ (\operatorname{GlcNAc-(Gal)}_{d^{-}} (\operatorname{Gal}_{d^{-}})_{h^{-}} (\operatorname$$

a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 43G

```
Insect cell expressed Urokinase.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- · 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-n = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 43H

```
Yeast expressed Urokinase.

a-n = 0;

q-y (independently selected) = 0 to 1;

p = 1; R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.
```

FIG. 431

```
CHO, BHK, 293 cells, Vero expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; n, v-y = 0.
```

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal1, desialylated Urokinase produced in CHO.
- 3. CMP-SA, ST3Gal3, ST3Gal1

```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-Urokinase.
```

FIG. 43J

```
Isolated Urokinase.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0; n = 0;

Sia (independently selected) = Sia or SO<sub>4</sub>;

Gal (independently selected) = Gal or GalNAc;

GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc.
```

sulfohydrolase
 CMP-SA-PEG, sialyltransferase

```
a-d, i-m, q-u (independently selected) = 0 or 1;
n = 0; e-h = 1; Sia = Sia;
Gal (independently selected) = Gal or GalNAc;
GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc.
v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 43K

Isolated Urokinase.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; n = 0; v-y = 0;

Sia (independently selected) = Sia or SO₄;

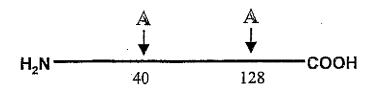
Gal (independently selected) = Gal or GalNAc;

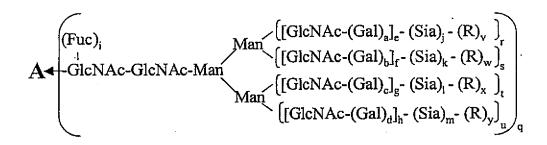
GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc.

- 1. sulfohydrolase, hexosaminidase
- 2. UDP-Gal-PEG, galactosyltransferase

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-n = 0; Gal (independently selected) = Gal; GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 43L





a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer, glycoconjugate.

FIG. 44A

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 44B

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 44C

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3
- 3. CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 44D

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

- CMP-SA-levulinate, ST3Gal3, buffer, salt
 H₄N₂-PEG
- a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

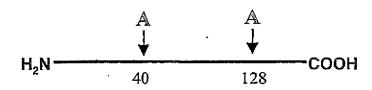
FIG. 44E

CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 44F



$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & & & \\ (\operatorname{Fuc})_{i} & & & \\ (\operatorname{GlcNAc-(Gal)}_{a}]_{e^{-}} (\operatorname{Sia})_{j^{-}} (\operatorname{R})_{v} \\ (\operatorname{GlcNAc-(Gal)}_{b}]_{f^{-}} (\operatorname{Sia})_{k^{-}} (\operatorname{R})_{w} \\ (\operatorname{R}')_{n} & & & \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{g^{-}} (\operatorname{Sia})_{i^{-}} (\operatorname{R})_{x} \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (\operatorname{R})_{y} \end{bmatrix}_{u}$$

a-d, i, n, p-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 6.
j-m (independently selected) = 0 to 100.
v-y = 0;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 44G

```
Insect cell expressed DNase I.
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT's 1,2,4,5, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1; j-n = 0;
v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 44H

```
Yeast expressed DNase I.

a-n = 0;

q-y (independently selected) = 0 to 1;

p = 1; R (branched or linear) = Man, oligomannose.
```

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-n, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

FIG. 441

CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; n, v-y=0.

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal1, desialylated alpha-1-Proteinase inhibitor.
- 3. CMP-SA, ST3Gal3, ST3Gal1

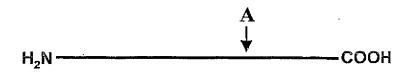
```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker- alpha-1-Proteinase inhibitor.
```

FIG. 44J



$$(Fuc)_{i} \\ A \leftarrow GlcNAc-Gal_{a}l_{e} - (Sia)_{j} - (R)_{v} \\ GlcNAc-Man \\ [GlcNAc-(Gal)_{b}l_{f} - (Sia)_{k} - (R)_{w}]_{s} \\ (R')_{n} \\ (R')_{n} \\ (GlcNAc-(Gal)_{c}l_{g} - (Sia)_{l} - (R)_{x} \\ [GlcNAc-(Gal)_{d}l_{h} - (Sia)_{m} - (R)_{y}]_{u} \\ [GlcNAc-(Gal)_{d}l_{h} - (Sia)_{m} - (R)_{y}]_{u} \\ (R')_{n} \\ (R')_{n}$$

a-d, i, r-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1;
R = modifying group, mannose, oligo-mannose;
R' = H, glycosyl residue, modifying group,
glycoconjugate.

FIG. 45A

```
CHO, BHK, 293 cells, Vero expressed Insulin.
a-m, r-u (independently selected) = 0 or 1;
n = 0; v-y = 0; z = 1.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-m, r-u (independently selected) = 0 or 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
n = 0; R = PEG; z = 1.
```

FIG. 45B

```
Insect cell expressed Insulin.
a-h, j-n, s-y = 0;
i, r (independently selected) = 0 or 1; z = 1.
```

1. GNT's 1&2, UDP-GlcNAc-PEG

```
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.
```

FIG. 45C

Yeast expressed Insulin.

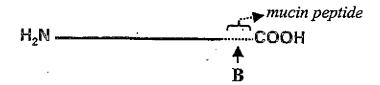
a-n=0; r-y (independently selected) = 0 to 1; z=1;

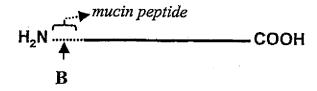
R (branched or linear) = Man, oligomannose or polysaccharide.

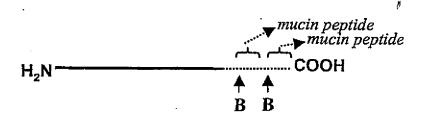
- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z= 0; n = 1; R' = -Gal-PEG.

FIG. 45D







$$\mathbf{B} = \left(\frac{(\operatorname{Sia})_{b}}{\operatorname{GalNAc-(Gal)}_{a} - (\operatorname{Sia})_{c} - (\operatorname{R})_{d}} \right)_{c}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer

FIG. 45E

CHO, BHK, 293 cells, Vero expressed insulinmucin fusion protein.

a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 45F

Insect cell expressed Insulin-mucin fusion protein. a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

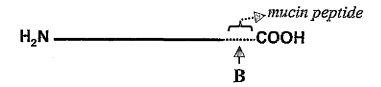
FIG. 45G

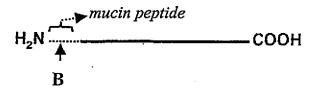
E. coli expressed Insulin-mucin fusion protein. a-e=0.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 45H





$$\mathbf{B} \leftarrow \begin{pmatrix} (\operatorname{Sia})_{b} \\ -\operatorname{GalNAc-(Gal)}_{a} - (\operatorname{Sia})_{c} - (R)_{d} \end{pmatrix}_{e}$$

$$\mathbf{C} \leftarrow (\mathbf{R}')_{\mathbf{n}}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = modifying group, mannose,oligo-mannose.

FIG. 451

E. coli expressed Insulin-mucin fusion protein. a-e, n=0.

1. GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 45J

E. coli expressed Insulin-mucin fusion protein. a-e, n = 0.

- GalNAc Transferase, UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

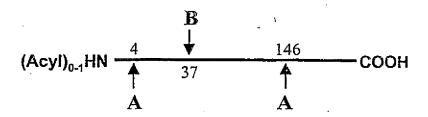
FIG. 45K

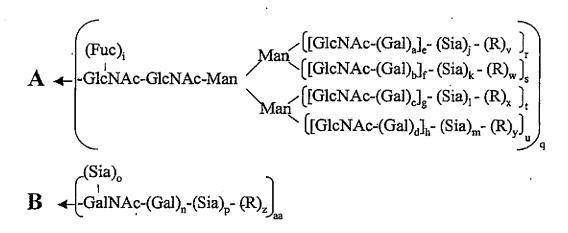
E. coli expressed Insulin (N)—no mucin peptide. a-e, n=0.

- 1. NHS-CO-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

a-e = 0; n = 1; R' = linker-transferrin.

FIG. 45L





a-d, i, n-u, aa (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer, glycoconjugate.

FIG. 46A

CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z=0.

- 1. Sialidase
- 2. CMP-SA-linker-lipid-A, ST3Gal3

```
a-d, i-m, q-u, aa (independently selected) = 0 or 1;
o, p, z = 0; n, e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = linker-lipid-A.
```

FIG. 46B

CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, as (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

- 1. sialidase
- 2. CMP-SA-linker-tetanus toxin, ST3Gal1
- 3. CMP-SA, ST3Gal3

a-d, i-m, p-u, z, as (independently selected) = 0 or 1; o, v-y=0; n, e-h=1; R= tetanus toxin.

FIG. 46C

```
NSO expressed M-antigen.
a-d, i-n, o-u, aa (independently selected) = 0 or 1;
e-h = 1; v-z = 0;
Sia (independently selected) = Sia or Gal.
```

- 1. α-galactosidase
- 2. CMP-SA, ST3Gal3
- 2. CMP-SA-KLH, ST3Gal1

```
a-d, i-n, p-u, z, as (independently selected) = 0 or 1;
e-h = 1; o, v-y = 0;
z = 1, when p = 1;
R = KLH.
```

FIG. 46D

```
Yeast expressed M-antigen.

a-p, z = 0; q-y, aa (independently selected) = 0 to 1;

R (branched or linear) = Man, oligomannose;

GalNAc = Man.
```

α1,2-mannosidase
 GNT 1,
 UDP-GlcNAc-linker-diphtheria toxin.

e, q, l, m, r, t, u, v, aa (independently selected) =0 or 1; a-d, f-h, j, k, n-p, s, w-z = 0; Sia = Man; R = linker-diphtheria toxin.

FIG. 46E

CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

- 1. CMP-SA-levulinate, ST3Gal3,
- 2. H₄N₂-linker-DNA

a-d, i-m, o-y, as (independently selected) = 0 or 1; z = 0; n, e-h = 1; R = linker-DNA.

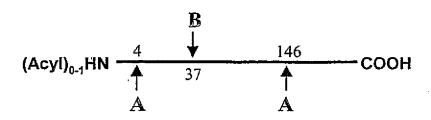
FIG. 46F

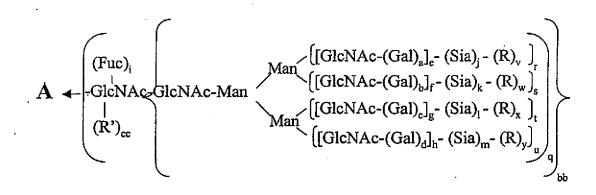
CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-n, o-u, aa (independently selected) = 0 or 1; e-h = 1; v-z = 0.

1. CMP-SA, poly-α2,8-ST

a-d, i, n-u, aa (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-100; v-z (independently selected) = 0.

FIG. 46G





$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{o} \\ -\mathrm{GalNAc-(Gal)}_{n} - (\mathrm{Sia})_{p} - (\mathrm{R})_{z} \end{bmatrix}_{aa}$$

a-d, i, n, q-u, aa, bb, (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-p (independently selected) = 0 to 100. Cc, v-y = 0; R = modifying group, mannose, oligo-mannose. R'= H, glycosyl residue, modifying group, glycoconjugate.

FIG. 46H

```
Insect cell expressed M-antigen.
a-d, f, h, j-m, o, p, s, u, v-z, cc = 0;
bb = 1;
e, g, i, n, q, r, t, aa (independently selected) = 0 or 1.
```

 GNT-2, UDP-GlcNAc-linker-Neisseria protein

```
a, c, e, g, i, n, q, r, t, v, x, aa (independently selected) = 0 or 1;
b, d, f, h, j-p, s, u, w, y, z, cc = 0;
bb = 1; R = -linker-Neisseria protein.
```

FIG. 46!

```
Yeast expressed M-antigen.

a-p, z, cc = 0;

q-y, aa (independently selected) = 0 to 1;

bb = 1; R (branched or linear) = Man, oligomannose;

GalNAc = Man.
```

1. Endoglycanase

2. Galactosyltransferase, UDP-Gal-linker-Neisseria protein

```
a-p, r-z, bb = 0;
q, aa, cc (independently selected) = 0 or 1;
R' = -Gal-linker-Neisseria protein.
```

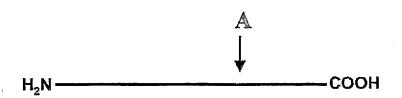
FIG. 46J

```
Yeast expressed M-antigen.
a-p, z, cc = 0;
q-y, aa (independently selected) = 0 to 1; bb = 1;
R (branched or linear) = Man, oligomannose;
GalNAc = Man.
```

- 1. mannosidases
- 2. GNT 1 & 2, UDP-GlcNAc
- 3. UDP-Gal, Galactosyltransferase,
- 4. CMP-SA, sialyltransferase

a, c, e, g, j, l, q, r, t, as (independently selected) = 0 or 1; b, d, f, h, k, m-p, s, u-z, cc = 0; bb = 1.

FIG. 46K



$$(Fuc)_{i} \\ A \leftarrow GlcNAc - GlcNAc - Man \\ \begin{bmatrix} [GlcNAc - (Gal)_{a}]_{e} - (Sia)_{j} - (R)_{v} \end{bmatrix}_{r} \\ [GlcNAc - (Gal)_{b}]_{f} - (Sia)_{k} - (R)_{w} \end{bmatrix}_{s} \\ (R')_{n} \\ \end{bmatrix}_{t} \\ \begin{bmatrix} [GlcNAc - (Gal)_{c}]_{g} - (Sia)_{l} - (R)_{x} \end{bmatrix}_{t} \\ \begin{bmatrix} [GlcNAc - (Gal)_{d}]_{h} - (Sia)_{m} - (R)_{y} \end{bmatrix}_{u} \\ \end{bmatrix}_{t} \\$$

a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 47A

CHO, BHK, 293 cells, Vero expressed Growth Hormone.

a-m, r-u (independently selected) = 0 or 1; n = 0; v-y = 0; z = 1.

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

a-m, r-u (independently selected) = 0 or 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; n = 0; R = PEG; z = 1.

FIG. 47B

```
Insect cell expressed growth hormone.
a-h, j-n, s-y = 0;
i, r (independently selected) = 0 or 1; z = 1.
```

I. GNT's 1&2, UDP-GlcNAc-PEG

```
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected)= 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.
```

FIG. 47C

Yeast expressed growth hormone.

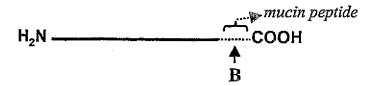
a-n = 0; r-y (independently selected) = 0 to 1; z = 1;

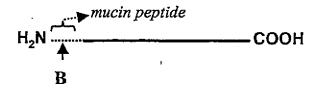
R (branched or linear) = Man, oligomannose or polysaccharide.

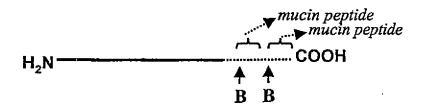
- I. Endo-H
- 2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z= 0; n = 1; R' = -Gal-PEG.

FIG. 47D







$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_b \\ -\mathrm{GalNAc} - (\mathrm{Gal})_a - (\mathrm{Sia})_c - (\mathrm{R})_d \end{bmatrix}_c$$

a-c, e (independently selected) = 0 or 1;
d = 0;
R = modifying group, mannose, oligomannose.

FIG. 47E

CHO, BHK, 293 cells, Vero expressed growth hormone-mucin fusion protein. a-c, e (independently selected) = 0 or 1; d = 0

I. Sialidase

2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 47F

Insect cell expressed Growth Hormone-mucin fusion protein.

a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

FIG. 47G

E. coli expressed growth hormone-mucin fusion protein.

a-e = 0.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 47H

E. coli expressed growth hormone-mucin fusion protein.

a-e, n=0.

1. GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 471

E. coli expressed growth hormone-mucin fusion protein.

a-e, n = 0.

- 1. GalNAc Transferase, UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- ▼ 3. CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

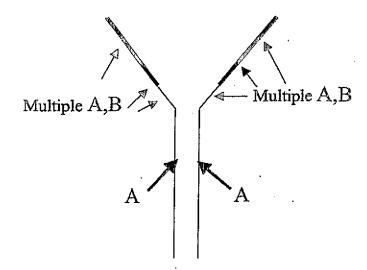
FIG. 47J

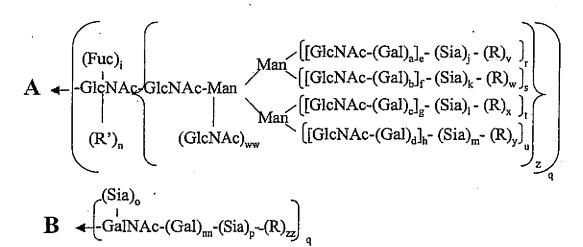
E. coli expressed growth hormone(N)—no mucin peptide.a-e, n = 0.

- 1. NHS-CO-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

a-e=0; n=1; R' = linker-transferrin.

FIG. 47K





a-d, i-m, q-u, w, z, nn, ww, zz (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4.

n, v-y = 0;

R = modifying group, mannose, oligo-mannose;

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 48A

CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion.

a-m, o-u, aa (independently selected) = 0 or 1;

n = 1; v-z = 0.

- 1. CMP-SA, ST3Gal1
- 2. galactosyltransferase, UPD-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, o-u, v-y, as (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

FIG. 48B

CHO, BHK, 293 cells, Vero expressed
TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.

1. sialidase
2. CMP-SA-PEG, ST3Gal1

a-i, p-u, z, aa (independently selected) = 0 or 1; n = 1; o, j-m, v-y = 0; R = PEG.

FIG. 48C

CHO, BHK, 293 cells, Vero expressed
TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.

 ${\tt 1.\ galactosyltransferase,\ UPD\text{-}Gal\text{-}PEG}$

a-m, o-u, v-y, as (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

FIG. 48D

CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion.

a-m, o-u, aa (independently selected) = 0 or 1;

n = 1; v-z = 0.

1. CMP-SA, ST3Gall
2. galactosyltransferase, UPD-Gal-PEG

a-m, o-u, v-y, aa (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

FIG. 48E

CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion.

a-m, o-u, aa (independently selected) = 0 or 1;

n = 1; v-z = 0.

1. CMP-SA-levulinate, ST3Gal12. H₄N₂-PEG

a-m, o-u, v-y, as (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

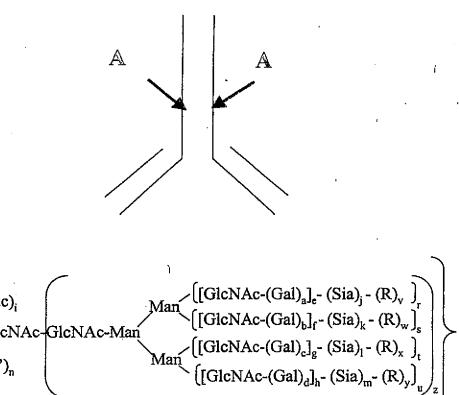
FIG. 48F

CHO, BHK, 293 cells, Vero expressed
TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.

1. CMP-SA-PEG, α 2,8-ST

a-i, o, q-u, v-z, aa (independently selected) = 0 or 1; n = 1; j-m, p (independently selected) = 0 to 2; v-z (independently selected) = 1, when j-m, p (independently selected) is 2; R = PEG.

FIG. 48G



a-d, i, l, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-k (independently selected) = 0 or 1.
M = 0 to 20.
n, v-y = 0; z = 0 or 1;
R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 49A

```
CHO, BHK, 293 cells, Vero expressed Herceptin.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;

q, z = 1.
```

- 1. galactosyltransferase, UPD-Gal
- 2. CMP-SA-toxin, ST3Gal3

```
a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1; R = toxin;
f, h, k, m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 51,
when j, l (independently selected) is l.
```

FIG. 49B

```
CHO, BHK, 293 cells, Vero or fungal expressed Herceptin.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;

q, z = 1.
```

 galactosyltransferase, UPD-Gal-Toxin

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = toxin.
```

FIG. 49C

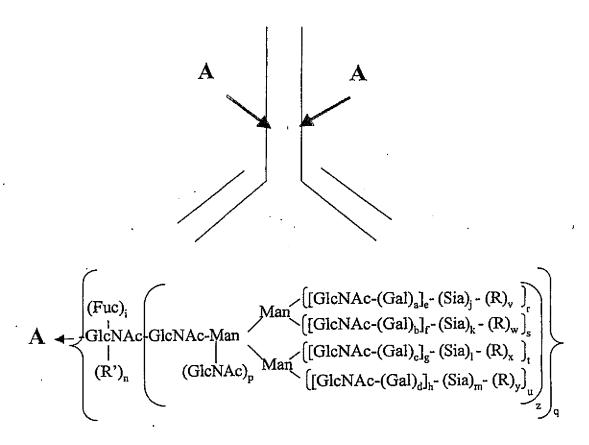
Fungi expressed Herceptin. e, g, i, r, t (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal

 3.. CMP-SA-radioisotope complex, ST3Gal3

a-m, r-z= 0; q, n = 1; R' = -Gal-Sia-radioisotope complex.

FIG. 49D



a-d, i, p-u, (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1;
R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 50A

```
CHO, BHK, 293 cells, Vero expressed Synagis.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1;

b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

- 1. galactosyltransferase, UPD-Gal
- 2. CMP-SA-PEG, ST3Gal3

```
a, c, i, j, w, (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when j, 1 (independently selected) is 1;
R = PEG.
```

FIG. 50B

```
CHO, BHK, 293 cells, Vero or fungal expressed Synagis.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;

q, z = 1.
```

 galactosyltransferase, UPD-Gal-PEG

```
a, c, i, w (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = PEG.
```

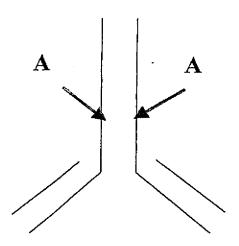
FIG. 50C

Fungi expressed Synagis. e, g, i, r, t (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- 3.. CMP-SA-PEG, ST3Gal3

a-m, r-z=0; q, n = 1; R' = -Gal-Sia-PEG.

FIG. 50D



$$\mathbf{A} \leftarrow \begin{array}{c} \text{(Fuc)}_{i} \\ \text{GlcNAc-Man} \\ \text{(R')}_{n} \end{array} \begin{array}{c} \text{(GlcNAc-(Gal)_{a}]_{e}-(Sia)_{j}-(R)_{v}} \\ \text{([GlcNAc-(Gal)_{b}]_{f}-(Sia)_{k}-(R)_{w}} \\ \text{([GlcNAc-(Gal)_{c}]_{g}-(Sia)_{l}-(R)_{x}} \\ \text{([GlcNAc-(Gal)_{d}]_{h}-(Sia)_{m}-(R)_{y}} \\ \text{([GlcNAc-(Gal)_{d}]_{h}-(Sia)_{m}-(R)_{y}} \\ \text{([GlcNAc-(Gal)_{d}]_{h}-(Sia)_{m}-(R)_{y}} \end{array}$$

a-d, i, q-u, w (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 20. n, v-y = 0; z = 0 or 1; R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 51A

```
CHO, BHK, 293 cells, Vero expressed Remicade.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;
q, z = 1.
```

- 1. galactosyltransferase, UPD-Gal
- 2. CMP-SA-PEG, ST3Gal3

```
a, c, i, j, 1 (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when j, 1 (independently selected) is 1;
R = PEG.
```

FIG. 51B

```
CHO, BHK, 293 cells, Vero or fungal expressed
Remicade.
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;
q, z = 1.
```

 galactosyltransferase, UPD-Gal-PEG

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = PEG.
```

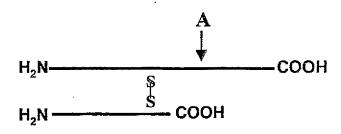
FIG. 51C

Fungi expressed Remicade. e, g, i, r, t (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

- 1. Endo-H
- Galactosyltransferase, UDP-Gal
 CMP-SA-radioisotope complex, ST3Gal3

a-m, r-z=0; q, n = 1; R' = -Gal-Sia-radioisotope complex.

FIG. 51D



$$\mathbf{A} \leftarrow \begin{array}{c} (\operatorname{Fuc})_{i} \\ \operatorname{GlcNAc-Man} \\ (\operatorname{R''})_{n} \end{array} \xrightarrow{\left[\left[\operatorname{GlcNAc-(Gal)}_{a} \right]_{e^{-}} \left(\operatorname{Sia})_{j^{-}} \left(\operatorname{R'}\right)_{v} \right]_{r}} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{b} \right]_{f^{-}} \left(\operatorname{Sia})_{k^{-}} \left(\operatorname{R'}\right)_{w} \right]_{s} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{c} \right]_{g^{-}} \left(\operatorname{Sia}\right)_{l^{-}} \left(\operatorname{R'}\right)_{v} \right]_{t} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia}\right)_{m^{-}} \left(\operatorname{R'}\right)_{y} \right]_{u^{-}} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia}\right)_{m^{-}} \left(\operatorname{R'}\right)_{y} \right]_{u^{-}} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia}\right)_{m^{-}} \left(\operatorname{R'}\right)_{y} \right]_{u^{-}} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia}\right)_{m^{-}} \left(\operatorname{R'}\right)_{y} \right]_{u^{-}} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia}\right)_{m^{-}} \left(\operatorname{R'}\right)_{y} \right]_{u^{-}} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia}\right)_{m^{-}} \left(\operatorname{R'}\right)_{y} \right]_{u^{-}} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia}\right)_{m^{-}} \left(\operatorname{R'}\right)_{y} \right]_{u^{-}} \\ \left[\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h^{-}} \left(\operatorname{Sia}\right)_{m^{-}} \left(\operatorname{R'}\right)_{y} \right]_{u^{-}} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia}\right)_{m^{-}} \left(\operatorname{Sia}\right)_{m^{-}} \left(\operatorname{R'}\right)_{y} \right]_{u^{-}} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia}\right)_{m^{-}} \left(\operatorname{R'}\right)_{y} \right]_{u^{-}} \\ \left[\operatorname{GlcNAc-(Gal)}_{d^{-}} \left(\operatorname{Sia}\right)_{m^{-}} \left(\operatorname{R'}\right)_{m^{-}} \right)_{u^{-}} \right]_{u^{-}}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 52A

```
CHO, BHK, 293 cells, Vero expressed Reopro. a-m, r-u (independently selected) = 0 or 1; n = 0; v-y = 0; z = 1.
```

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal3

```
a-m, r-u (independently selected) = 0 or 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
n = 0; R = PEG; z = 1.
```

FIG. 52B

```
Insect cell expressed Reopro.

a-h, j-n, s-y = 0; i, r (independently selected) = 0 or 1;

z = 1.
```

1. GNT's 1&2, UDP-GlcNAc-PEG

```
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.
```

FIG. 52C

```
Yeast expressed Reopro.

a-n = 0; r-y (independently selected) = 0 to 1;

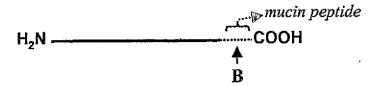
z = 1;

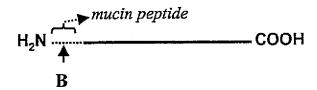
R (branched or linear) = Man, oligomannose or polysaccharide.
```

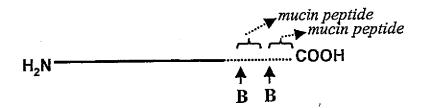
- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z= 0; n = 1; R' = -Gal-PEG.

FIG. 52D







$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc-(Gal)}_{a} - (\mathrm{Sia})_{c} - (\mathrm{R})_{d} \end{bmatrix}_{c}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer

FIG. 52E

CHO, BHK, 293 cells, Vero expressed
Reopro-mucin fusion protein.
a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 52F

Insect cell expressed Reopro-mucin fusion protein. a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

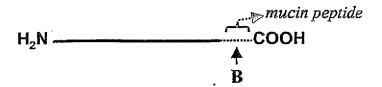
FIG. 52G

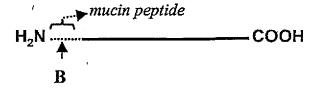
E. coli expressed Reopro-mucin fusion protein. a-e = 0.

- 1. GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 52H





$$\mathbf{B} \quad \bullet \begin{array}{c} \text{(Sia)}_{b} \\ \text{-GalNAc-(Gal)}_{a}\text{-(Sia)}_{c}\text{- (R)}_{d} \\ \\ \end{array}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer, linker.

FIG. 521

E. coli expressed Reopro-mucin fusion protein. a-e, n = 0.

1. GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 52J

E. coli expressed Reopro-mucin fusion protein. a-e, n=0.

- GalNAc Transferase, UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

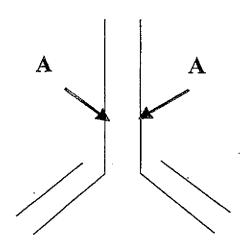
FIG. 52K

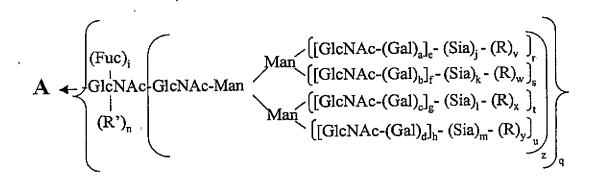
E. coli expressed Reopro(N)—no mucin peptide. a-e, n = 0.

- 1. NHS-CO-linker-SA-CMP
- ST3Gal3, asialo-transferrin
 CMP-SA, ST3Gal3

a-e=0; n=1; R'=linker-transferrin.

FIG. 52L





a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = polymer, toxin, radioisotopecomplex, drug, glycoconjugate. R' = H, sugar, glycoconjugate.

FIG. 53A

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed Rituxan.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

1. galactosyltransferase, UPD-Gal

2. CMP-SA-toxin, ST3Gal3

```
a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1;
f, h, k, m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 1,
when j, l (independently selected) is 1;
R = toxin.
```

FIG. 53B

```
CHO, BHK, 293 cells, Vero or fungal expressed Rituxan.

a, c, e, g, i, r, t (independently selected) = 0 or 1;

b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

1. galactosyltransferase, UPD-Gal-drug

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, j-m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = toxin.
```

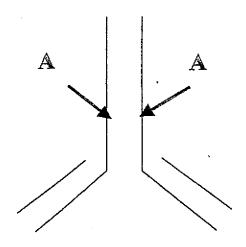
FIG. 53C

```
Fungi expressed Rituxan.
e, g, i, r, t (independently selected) = 0 or 1;
a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal3. CMP-SA-radioisotope complex, ST3Gal3

```
a-m, r-z= 0; q, n = 1;
R' = -Gal-Sia-radioisotope complex.
```

FIG. 53D



$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & & & & & & & & & & & & & \\ (\operatorname{Fuc})_{i} & & & & & & & & & & \\ (\operatorname{GlcNAc-(Gal)}_{a}]_{e}^{-} & (\operatorname{Sia})_{j}^{-} & (\operatorname{R})_{v} & & & & \\ (\operatorname{GlcNAc-(Gal)}_{b}]_{f}^{-} & (\operatorname{Sia})_{k}^{-} & (\operatorname{R})_{w} & & & \\ (\operatorname{GlcNAc-(Gal)}_{c}]_{g}^{-} & (\operatorname{Sia})_{i}^{-} & (\operatorname{R})_{x} & & \\ (\operatorname{R'})_{n} & & & & & & & \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{h}^{-} & (\operatorname{Sia})_{m}^{-} & (\operatorname{R})_{y} & & \\ & & & & & & & \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{h}^{-} & (\operatorname{Sia})_{m}^{-} & (\operatorname{R})_{y} & & \\ & & & & & & \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h}^{-} & (\operatorname{Sia})_{m}^{-} & (\operatorname{R})_{y} & & \\ & & & & & & \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h}^{-} & (\operatorname{Sia})_{m}^{-} & (\operatorname{R})_{y} & & \\ & & & & & & \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h}^{-} & (\operatorname{Sia})_{m}^{-} & (\operatorname{R})_{y} & & \\ & & & & & \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h}^{-} & (\operatorname{Sia})_{m}^{-} & (\operatorname{R})_{y} & & \\ & & & & & \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h}^{-} & (\operatorname{Sia})_{m}^{-} & (\operatorname{R})_{y} & & \\ & & & & & \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h}^{-} & (\operatorname{Sia})_{m}^{-} & (\operatorname{R})_{y} & & \\ & & & & \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h}^{-} & (\operatorname{Sia})_{m}^{-} & (\operatorname{R})_{y} & & \\ & & & & \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h}^{-} & (\operatorname{Sia})_{m}^{-} & (\operatorname{R})_{y} & & \\ & & & & \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h}^{-} & (\operatorname{Sia})_{m}^{-} & (\operatorname{R})_{y} & & \\ & & & & \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h}^{-} & (\operatorname{Sia})_{m}^{-} & (\operatorname{R})_{y} & & \\ & & & & \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h}^{-} & (\operatorname{Sia})_{m}^{-} & (\operatorname{R})_{m}^{-} & (\operatorname{R})_{m}^{-} & (\operatorname{Sia})_{m}^{-} & (\operatorname{R})_{m}^{-} & (\operatorname{R})_{m}^$$

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1;
R = polymer, toxin, radioisotope-complex, drug, glycoconjugate, mannose, oligo-mannose.
R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 53E

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed Rituxan.

a, c, i (independently selected) = 0 or 1;

e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0;

q, z = 1.
```

- 1. galactosyltransferase, UPD-Gal
- 2. CMP-SA-PEG, ST3Gal3

```
a, c, i, j, 1 (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when j, 1 (independently selected) is 1;
R = PEG.
```

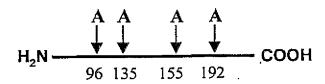
FIG. 53F

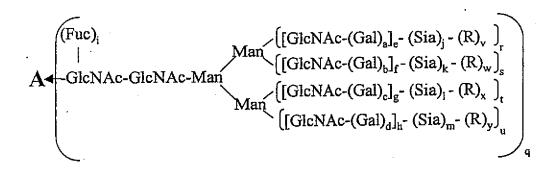
```
Fungi, yeast or CHO expressed Rituxan.
e, g, i, r, t, v, x (independently selected) = 0 or 1;
a-d, f, h, j-m, n, s, u, w, y = 0; q, z = 1;
R (independently selected) = mannose, oligomannose, polymannose.
```

- 1. mannosidases (alpha and beta)
- 2. GNT-I,II, UDP-GlcNAc
- 3. Galactosyltransferase, UDP-Gal-radioisotope

```
a-m, r-z=0; q, n = 1;
R' = -Gal-radioisotope complex.
```

FIG. 53G





a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = mannose, polymer.

FIG. 54A

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed AT III. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 54B

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed AT III.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0.
```

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 54C

```
NSO expressed AT III.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α -galactosidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 54D

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed AT III.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq),
ST3Gal3
3. CMP-SA, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1;
```

v-y (independently selected) = 0 or 1;

FIG. 54E

e-h = 1;

R = PEG.

CHO, BHK, 293 cells, Vero or transgenic animal expressed AT III.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0.

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H₄N₂-PEG

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

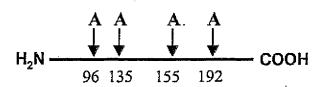
FIG. 54F

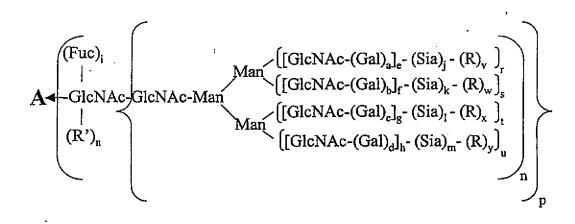
CHO, BHK, 293 cells, Vero expressed AT III. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

1. CMP-SA, poly- α 2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 54G





a-d, i, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0 to 100. R = polymer, linker, mannose. R' = H, sugar, glycoconjugate.

FIG. 54H

```
Insect, yeast or fungi cell expressed AT III.

a-d, f, h, j-n, s, u, v-y = 0;

e, g, i, q, r, t (independently selected) = 0 or 1;

p = 1.
```

1. GNT 1, UDP-GlcNAc-PEG

```
a, i, q, r, -u (independently selected) = 0 or 1;
b-g, j-n, s-u, w-y = 0; p = 1;
v (independently selected) = 1,
when a (independently selected) is 1;
R = PEG.
```

FIG. 541

```
Yeast expressed AT III.

a-n = 0; q-y (independently selected) = 0 to 1;

p = 1;

R (branched or linear) = Man, oligomanmose.
```

- Endoglycanase
 Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0;
n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.
```

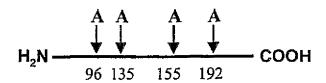
FIG. 54J

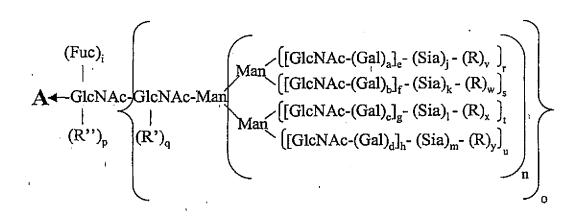
CHO, BHK, 293 cells, Vero expressed AT III. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

- 1. CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, transferrin treated with endoglycanase

a-m, q-u (independently selected) = 0 or 1; p = 1; n = 0; v-y (independently selected) = 0 or 1; R = linker-transferrin.

FIG. 54K





a-d, i, n-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 to 20.

R = polymer.

R', R" (independently selected) = sugar, glycoconjugate.

FIG. 54L

```
Yeast expressed AT III.

a-h, i-m, p, q = 0;

R (independently selected) = mannose,
oligomannose, polymannose;

r-u, v-y (independently selected) = 0 or 1;

n, o = 1.
```

1. endoglycanase

▼ 2. Galactosyltransferase, UDP-Gal-PEG

```
a-h, i-o, q, r-u, v-y = 0; p = 1.
R" = Gal-PEG.
```

FIG. 54M

```
Plant expressed AT III.

a-d, f-h, j-m, p, s-u, v-y = 0;

e, i, q, r (independently selected) = 0 or 1;

n, o = 1; R' = xylose.
```

1. xylosidase

3. Galactosyl transferase, UDP-Gal-PEG

```
b-d, f-h, j-m, p, q, s-u, w-y = 0;
a, e, i, r (independently selected) = 0 or 1;
n, o = 1; R = PEG.
```

FIG. 54N

CHO, BHK, 293 cells, Vero, transgenic animal expressed AT III.

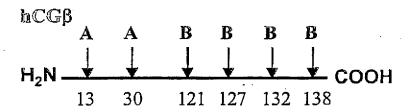
a-h, i-o, r-u (independently selected) = 0 or 1;

p, q, v-y = 0.

1. CMP-SA-PEG, ST3Gal3

a-h, i-o, r-u (independently selected) = 0 or 1; p, q = 0; v-y (independently selected) = 0 or 1; R = PEG.

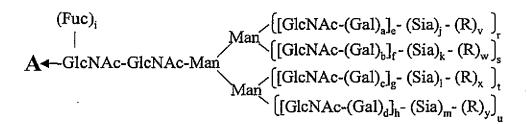
FIG. 540



hCG
$$\alpha$$

$$H_2N$$

$$52 78$$
A A
$$\downarrow \downarrow \downarrow$$
COOH



$$\mathbf{B}$$
GalNAc-(Gal)_n-(Sia)_p- (R)_z

a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. v-z = 0; R = polymer

FIG. 55A

CHO, BHK, 293 cells, insect cell, Vero expressed hCG
a-g, n, q = 1; h = 1 to 3; j-m, i, o, p
(independently selected) = 0 or 1; r-u
(independently selected) = 0 to1; v-z = 0

Sialidase

2. CMP-SA-PEG, ST3Gal3

a-g, n, q = 1; h = 1 to 3; i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; j-m, v-y (independently selected) = 0 or 1; R = PEG; z = 0.

FIG. 55B

Insect cell, yeast, fungi expressed hCG a-d, f, h, j-m, o, p, s, u, v-z = 0; e, g, i, n, q, r, t (independently selected) = 0 or 1.

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal
- 2. CMP-SA-PEG, ST3Gal3

b, d, f, h, k, m, o, p, s, u, w, y, z = 0;
a, c, e, g, i, n, q, r, t (independently selected)
= 0 or 1;
j, l, v, x (independently selected) = 0 or 1;
R = PEG.

FIG. 55C

```
CHO, BHK, 293 cells, insect cell,
Vero expressed hCG
a-q, r-u (independently selected) = 0 or 1;
v-z = 0.
```

- 1. sialidase
- 2. CMP-SA, ST3Gal3
- 3. CMP-SA-PEG, ST3Gal1

```
a-h, i-o, q, r-u (independently selected) = 0 or 1;
v-y = 0; p, z = 0 or 1; R = PEG.
```

FIG. 55D

```
CHO, BHK, 293 cells, insect cell or

Vero expressed hCG

a-g, n, q = 1; h = 1 to 3;

j-m, i, o, p (independently selected) = 0 or 1;

r-u (independently selected) = 0 or 1; v-z = 0
```

1. CMP-SA-PÉG, ST3Gal3

```
a-g, n, q = 1; h = 1 to 3;

i, o, p (independently selected) = 0 or 1;

r-u (independently selected) = 0 to 1;

j-m, v-y (independently selected) = 0 or 1;

R = PEG; z = 0.
```

FIG. 55E

Insect cell, yeast or fungi expressed hCG a-d, f, h, j-m, o, p, s, u, v-z = 0; e, g, i, n, q, r, t (independently selected) = 0 or 1.

1. GNT's 1 and 2, UDP-GlcNAc-PEG

e, g, i, n, q, r, t, v, x (independently selected) = 0 or 1; a-d, f, h, j-m, o, p, s, w, y, z = 0; R = PEG.

FIG. 55F

Insect cell, yeast or fungi expressed hCG a-d, f, h, j-m, o, p, s, u, v-z = 0; e, g, i, n, q, r, t (independently selected) = 0 or 1.

1. GNT-1 , UDP-GlcNAc-PEG

e, i, n, q, r, v (independently selected) = 0 or 1; a-d, g, f, h, j-m, o, p, s, t, w-z = 0; R = PEG.

FIG. 55G

```
CHO, BHK, 293 cells, insect cell or

Vero expressed hCG

a-g, n, q = 1; h = 1 to 3;

j-m, i, o, p (independently selected) = 0 or 1;

r-u (independently selected) = 0 or 1; v-z = 0

1. CMP-SA-PEG, ST3Gal3
```

```
a-g, n, q = 1; h = 1 to 3;

i, o (independently selected) = 0 or 1;

r-u (independently selected) = 0 to 1;

j-m, p, z (independently selected) = 0 or 1;

R = PEG; v-y = 0.
```

FIG. 55H

```
CHO, BHK, 293 cells, Vero expressed hCG a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; v-z = 0
```

1. CMP-SA-PEG, α2,8-ST

```
a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1;
j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1, when j-m
(independently selected) is 2; R = PEG; z = 0.
```

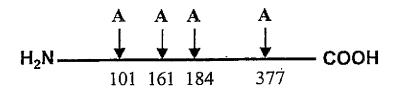
FIG. 551

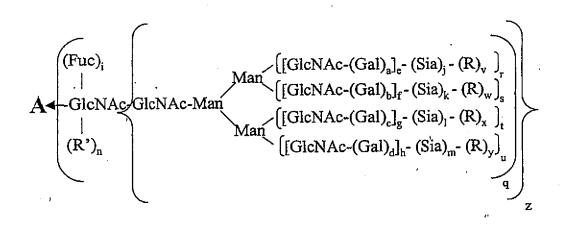
```
CHO, BHK, 293 cells, Vero expressed hCG
a-g, n, q = 1; h = 1 to 3;
j-m, i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1; v-z = 0

1. CMP-SA, poly-α2,8-ST

a-i, j-q, r-u, (independently selected) = 0 or 1;
v-z (independently selected) = 0-100; R = Sia.
```

FIG. 55J





a-d, i, n, q-u, z (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0 to 100; R = mannose, mannose-6-phosphate and mannose, polymer.

FIG. 56A

```
CHO, BHK, 293 cells, insect cells, Vero expressed and secreted alpha-galactosidase a-h, i-m, q-u (independently selected) = 0 or 1; z = 1; n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.
```

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal-PEG-transferrin

```
a-h, i-m, q-u (independently selected) = 0 or 1;

n, v-y = 0; z = 1; and when z = 0 and q = 1,

then n (independently selected) = 0 or 1;

R' = Gal-PEG-transferrin.
```

FIG. 56B

```
CHO, BHK, 293 cells, Insect cells,

Vero expressed and secreted alpha-galactosidase
a-h, i-m, q-u (independently selected) = 0 or 1; z = 1; n, v-y
= 0; and when a-n = 0, then r-u (independently selected) = 0
or 1; v-y (independently selected) = 0-100;
R = mannose or mannose with mannose-6-phosphate.
```

- 1. Sialidase
 2. CMP-SA-linker-Mannose-6-phosphate
 ST3Gal3
- a-h, i-m, q-u, v-y (independently selected) = 0 or 1; n = 0; z=1; R = mannose-6-phosphate; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.

FIG. 56C

NSO expressed alpha-galactosidase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0; Sia (independently selected) = Sia or Gal.

- 1. Sialidase and α-galactosidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-linker-mannose-6-phosphate sialyltransferase

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; R = mannose-6 phosphate

FIG. 56D

CHO, BHK, 293 cells, Insect cells, Vero expressed and secreted alpha-galactosidase a-h, i-m, q-u (independently selected) = 0 or 1; z = 1; n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.

- 1. Sialidase
- 2. CMP-SA-PEG, sialyltransferase

a-h, i-m, q-u, v-y (independently selected) = 0 or 1; n = 0; z = 1; R = PEG; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y = 0-100; R = mannose or mannose with mannose-6-phosphate.

FIG. 56E

```
CHO, BHK, 293 cells, Insect cells, Vero, yeast, fungi expressed alpha-galactosidase.

a-i, v-y = 0; q (independently selected) = 0 or 1; z = 1; r-u (independently selected) = 0 or 1; j-m (independently selected) = 0-100; Sia = mannose or mannose with mannose-6-phosphate.
```

1. mannosyltransferase, GDP-mannose-linker-ApoE

```
a-i = 0; q (independently selected) = 0 or 1; z = 1;
r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0-100;
Sia = mannose or mannose with mannose-6-phosphate;
v-y (independently selected) = 0 or 1;
R = mannose-linker-ApoE.
```

FIG. 56F

```
CHO, BHK, 293 cells, Insect cells, Vero, yeast, fungi expressed alpha-galactosidase.

a-i, v-y = 0; q (independently selected) = 0 or 1; z = 1; r-u (independently selected) = 0 or 1; j-m (independently selected) = 0-100; Sia = mannose or mannose with mannose-6-phosphate.
```

1. endo-H

2. galactosyltransferase, UDP-Gal-linker-alpha2-macroglobulin

a-m, r-z=0; n, q (independently selected) = 0 or 1; R' = galacotose-linker-alpha2-macroglobulin.

FIG. 56G

```
Insect cell, yeast, fungi expressed
alpha-galactosidase.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT-1,
UDP-GlcNAc-PEG-mannose-6-phosphate

e, i, q, r, v (independently selected) = 0 or 1;
a-d, f-h, j-n, s-u, w-y = 0; z = 1;
R = PEG-mannose-6-phosphate.
```

FIG. 56H

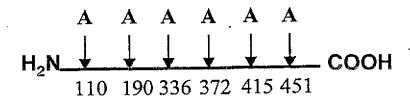
FIG. 561

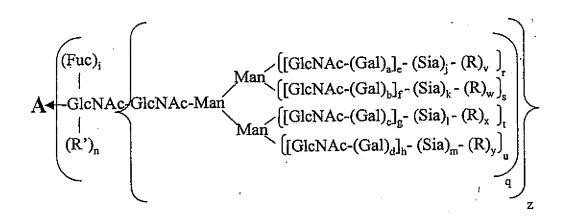
Insect cell, yeast, fungi expressed
alpha-galactosidase.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

- 1. GNT-1 and 2, UDP-GlcNAc
- 2. galactosyltransferase, UDP-Gal
- 3. sialyltransferase, CMP-SA-PEG-melanotransferrin

a, c, e, g, i, j, l, q, r, t, v, x (independently selected) = 0 or 1;
b, d, f, h, k, m, n, s, u, w, y = 0;
z = 1; R = PEG-melanotransferrin.

FIG. 56J





a-d, i, n, q-u, z (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0 to 100; R = mannose, mannose-6-phosphate and mannose, polymer.

FIG. 57A

```
cho, BHK, 293 cells, Insect cells, Vero expressed and secreted alpha-iduronidase a-h, i-m, q-u (independently selected) = 0 or 1; z = 1; n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.
```

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal-PEG-transferrin

```
a-h, i-m, q-u (independently selected) \stackrel{.}{=} 0 or 1;
n, v-y = 0; z = 1; and when z = 0 and q = 1, then n
(independently selected) = 0 or 1; R' = Gal-PEG-transferrin.
```

FIG. 57B

```
CHO, BHK, 293 cells, Insect cells, Vero expressed and secreted alpha-iduronidase a-h, i-m, q-u (independently selected) = 0 or 1; z = 1; n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.
```

- 1. Sialidase
- 2. CMP-SA-linker-Mannose-6-phosphate ST3Gal3

```
a-h, i-m, q-u, v-y (independently selected) = 0 or 1; n = 0; z = 1; R = mannose-6-phosphate; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.
```

FIG. 57C

```
NSO expressed alpha-iduronidase.

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1;

v-y = 0; Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-linker-mannose-6-phosphate sialyltransferase

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = mannose-6 phosphate
```

FIG. 57D

```
cho, BHK, 293 cells, Insect cells, Vero expressed and secreted alpha-iduronidase a-h, i-m, q-u (independently selected) = 0 or 1; z = 1; n, v-y = 0; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y (independently selected) = 0-100; R = mannose or mannose with mannose-6-phosphate.
```

- 1. Sialidase
- 2. CMP-SA-PEG, sialyltransferase

```
a-h, i-m, q-u, v-y (independently selected) = 0 or 1; n = 0; z = 1; R = PEG; and when a-n = 0, then r-u (independently selected) = 0 or 1; v-y = 0-100; R = mannose or mannose with mannose-6-phosphate.
```

FIG. 57E

```
CHO, BHK, 293 cells, Insect cells, Vero, yeast, fungi expressed alpha-iduronidase.

a-i, v-y = 0; q (independently selected) = 0 or 1; z = 1; r-u (independently selected) = 0 or 1; j-m (independently selected) = 0-100; Sia = mannose or mannose with mannose-6-phosphate.
```

1. mannosyltransferase, GDP-mannose-linker-ApoE

```
a-i = 0; q (independently selected) = 0 or 1; z = 1;
r-u (independently selected) = 0 or 1; j-m (independently
selected) = 0-100;
Sia = mannose or mannose with mannose-6-phosphate;
v-y (independently selected) = 0 or 1;
R = mannose-linker-ApoE.
```

FIG. 57F

```
CHO, BHK, 293 cells, Insect cells, Vero, yeast, fungi expressed alpha-iduronidase.

a-i, v-y = 0; q (independently selected) = 0 or 1;

z = 1; r-u (independently selected) = 0 or 1;

j-m (independently selected) = 0-100;

Sia = mannose or mannose with mannose-6-phosphate.
```

1. endo-H

2. galactosyltransferase, UDP-Gal-linker-alpha2-macroglobulin

a-m, r-z = 0; n, q (independently selected) = 0 or 1; R' = galacotose-linker-alpha2-macroglobulin.

FIG. 57G

```
Insect cell, yeast, fungi expressed
alpha-iduronidase.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT-1,
UDP-GlcNAc-PEG-mannose-6-phosphate

e, i, q, r, v (independently selected) = 0 or 1;
a-d, f-h, j-n, s-u, w-y = 0; z = 1;
R = PEG-mannose-6-phosphate.
```

FIG. 57H

FIG. 571

```
Insect cell, yeast, fungi expressed
alpha-iduronidase.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

- 1. GNT-1 and 2, UDP-GlcNAc
 2. galactosyltransferase, UDP-Gal
 3. sialyltransferase,
 CMP-SA-PEG-melanotransferrin
- a, c, e, g, i, j, l, q, r, t, v, x (independently selected) = 0 or 1; b, d, f, h, k, m, n, s, u, w, y = 0; z = 1; R = PEG-melanotransferrin.

FIG. 57J

FIG. 58A

FIG. 58B

Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro

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GCGCCTCTTATGTACCCACAAAAATCTATTTTCAAAAAAGTTGCTCTA AGAATATAGTTATCAAGTTAAGTAAAATGTCAATAGCCTTTTAATTTA ATTTTTAATTGTTTTATCATTCTTTGCAATAATAAAACATTAACTTTAT ACTTTTTAATTTAATGTATAGAATAGAGATATACATAGGATATGTAAA TAGATACACAGTGTATATGTGATTAAAATATAATGGGAGATTCAATC AATAATGAAAAAATGTGGTGAGAAAACAGCTGAAAACCCATGTA AAGAGTGTATAAAGAAAGCAAAAAGAGAAGTAGAAAGTAACACAGG GGCATTTGGAAAATGTAAACGAGTATGTTCCCTATTTAAGGCTAGGC ACAAAGCAAGGTCTTCAGAGAACCTGGAGCCTAAGGTTTAGGCTCAC CCATTTCAACCAGTCTAGCAGCATCTGCAACATCTACAATGGCCTTGA CCTTTGCTTTACTGGTGCCCTCCTGGTGCTCAGCTGCAAGTCAAGCT GCTCTGTGGGCTGTGATCTGCCTCAAACCCACAGCCTGGGTAGCAGG AGGACCTTGATGCTCCTGGCACAGATGAGGAGAATCTCTCTTTTCTCC TGCTTGAAGGACAGACATGACTTTGGATTTCCCCAGGAGGAGTTTGG CAACCAGTTCCAAAAGGCTGAAACCATCCCTGTCCTCCATGAGATGA TCCAGCAGATCTTCAATCTCTTCAGCACAAAGGACTCATCTGCTGCTT GGGATGAGACCCTCCTAGACAAATTCTACACTGAACTCTACCAGCAG CTGAATGACCTGGAAGCCTGTGTGATACAGGGGGTGGGGGTGACAGA GACTCCCCTGATGAAGGAGGACTCCATTCTGGCTGTGAGGAAATACT TCCAAAGAATCACTCTCTATCTGAAAGAGAAGAAATACAGCCCTTGT GCCTGGGAGGTTGTCAGAGCAGAAATCATGAGATCTTTTTCTTTGTCA ACAAACTTGCAAGAAAGTTAAGAAGTAAGGAATGAAAACTGGTTCA ACATGGAAATGATTTCATTGATTCGTATGCCAGCTCACCTTTTTATG ATCTGCCATTTCAAAGACTCATGTTTCTGCTATGACCATGACACGATT TAAATCTTTTCAAATGTTTTTAGGAGTATTAATCAACATTGTATTCAG ATCTATTTAAATATTTTTAAAATATTATTTATTTAACTATTTATAAAAAC AACTTATTTTTGTTCATATTATGTCATGTGCACCTTTGCACAGTGGTTA CATTGAACTTTTGCTATGGAACTTTTGTACTTGTTTATTCTTTAAAATG AAATTCCAAGCCTAATTGTGCAACCTGATTACAGAATAACTGGTACA CTTCATTTGTCCATCAATATTATATTCAAGATATAAGTAAAAATAAAC TTTCTGTAAACCAAGTTGTATGTTGTACTCAAGATAACAGGGTGAACC TAACAAATACAATTCTGCTCTCTTGTGTATTTGATTTTTGTATGAAAA AAACTAAAAATGGTAATCATACTTAATTATCAGTTATGGTAAATGGT ATGAAGAGAAGAAGGAACG

FIG. 59B

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Met Ala Leu Thr Phe Ala Leu Leu Val Ala Leu Val Leu Ser Cys Lys Ser Ser Cys Ser Val Gly Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu

FIG. 59C

FIG. 59D

Met Ala Leu Leu Phe Pro Leu Leu Ala Ala Leu Val Met Thr Ser Tyr Ser Pro Val Gly Ser Leu Gly Cys Asp Leu Pro Gln Asn His Gly Leu Leu Ser Arg Asn Thr Leu Val Leu His Gln Met Arg Arg Ile Ser Pro Phe Leu Cys Leu Lys Asp Arg Arg Asp Phe Arg Phe Pro Gln Glu Met Val Lys Gly Ser Gln Leu Gln Lys Ala His Val Met Ser Val Leu His Glu Met Leu Gln Gln Ile Phe Ser Leu Phe His Thr Glu Arg Ser Ser Ala Ala Trp Asn Met Thr Leu Leu Asp Gln Leu His Thr Gly Leu

FIG. 60A

ATGACCAACAAGTGTCTCCTCCAAATTGCTCTCCTGTTGTGCTTCTCC ACTACAGCTCTTTCCATGAGCTACAACTTGCTTGGATTCCTACAAAGA AGCAGCAATTTTCAGTGTCAGAAGCTCCTGTGGCAATTGAATGGGAG GCTTGAATATTGCCTCAAGGACAGGATGAACTTTGACATCCCTGAGG AGATTAAGCAGCTGCAGCAGTTCCAGAAGGAGGACGCCGCATTGACC ATCTATGAGATGCTCCAGAACATCTTTGCTATTTTCAGACAAGATTCA TCTAGCACTGGCTGGAATGAGACTATTGTTGAGAACCTCCTGGCTAA TGTCTATCATCAGATAAACCATCTGAAGACAGTCCTGGAAGAAAAAC TGGAGAAAGAATTTTACCAGGGGAAAACTCATGAGCAGTCTGCAC CTGAAAAGATATTATGGGAGGATTCTGCATTACCTGAAGGCCAAGGA GTACAGTCACTGTGCCTGGACCATAGTCAGAGTGGAAATCCTAAGGA ACTTTTACTTCATTAACAGACTTACAGGTTACCTCCGAAACTGAAGAT CTCCTAGCCTGTCCCTCTGGGACTGGACAATTGCTTCAAGCATTCTTC AACCAGCAGATGCTGTTTAAGTGACTGATGGCTAATGTACTGCAAAT GAAAGGACACTAGAAGATTTTGAAATTTTTATTAAATTATGAGTTATT TTTATTTAT TTAAATTTTATTTTGGAAAATAAATTATTTTTGGTGC

FIG. 60B

Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Cys Phe Ser Thr Thr Ala Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly ArgLeu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn

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FIG. 61A

ATGGTCTCCCAGGCCCTCAGGCTCCTCTGCCTTCTGCTTGGGCTTCAG GGCTGCCTGGCTGCAGTCTTCGTAACCCAGGAGGAAGCCCACGGCGT CCTGCACCGGCGCGCGCGCCAACGCGTTCCTGGAGGAGCTGCGGC CGGGCTCCCTGGAGAGGGAGTGCAAGGAGGAGCAGTGCTCCTTCGA GGAGGCCCGGGAGATCTTCAAGGACGCGGAGAGGACGAAGCTGTTC TGGATTTCTTACAGTGATGGGGACCAGTGTGCCTCAAGTCCATGCCA GAATGGGGGCTCCTGCAAGGACCAGCTCCAGTCCTATATCTGCTTCT GCCTCCCTGCCTTCGAGGGCCGGAACTGTGAGACGCACAAGGATGAC CAGCTGATCTGTGAACGAGAACGGCGGCTGTGAGCAGTACTGCAG TGACCACACGGGCACCAAGCGCTCCTGTCGGTGCCACGAGGGGTACT CTCTGCTGGCAGACGGGGTGTCCTGCACACCCACAGTTGAATATCCA TGTGGAAAAATACCTATTCTAGAAAAAAGAAATGCCAGCAAACCCCA AGGCCGAATTGTGGGGGGCAAGGTGTGCCCCAAAGGGGAGTGTCCA TGGCAGGTCCTGTTGTTGGTGAATGGAGCTCAGTTGTGTGGGGGGAC CCTGATCAACACCATCTGGGTGGTCTCCGCGGCCCACTGTTTCGACAA AATCAAGAACTGGAGGAACCTGATCGCGGTGCTGGGCGAGCACGAC CTCAGCGAGCACGACGGGGATGAGCAGAGCCGGCGGGTGGCGCAGG GCGCTGCTCCGCCTGCACCAGCCCGTGGTCCTCACTGACCATGTGGTG CCCCTCTGCCTGCCCGAACGGACGTTCTCTGAGAGGACGCTGGCCTTC GTGCGCTTCTCATTGGTCAGCGGCTGGGGCCAGCTGCTGGACCGTGG CGCCACGGCCCTGGAGCTCATGGTGCTCAACGTGCCCCGGCTGATGA CCCAGGACTGCCTGCAGCAGTCACGGAAGGTGGGAGACTCCCCAAAT ATCACGGAGTACATGTTCTGTGCCGGCTACTCGGATGGCAGCAAGGA GCACGTGGTACCTGACGGCCATCGTCAGCTGGGGCCAGGGCTGCGCA ACCGTGGGCCACTTTGGGGTGTACACCAGGGTCTCCCAGTACATCGA GTGGCTGCAAAAGCTCATGCGCTCAGAGCCACGCCCAGGAGTCCTCC TGCGAGCCCCATTTCCC

FIG. 61B

Met Val Ser Gln Ala Leu Arg Leu Leu Cys Leu Leu Leu Gly Leu Gln Gly Cys Leu Ala Ala Val Phe Val Thr Gln Glu Glu Ala His Gly Val Leu His Arg Arg Arg Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro Gly Ser Leu Glu Arg Glu Cys Lys Glu Glu Glu Cys Ser Phe Glu Glu Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg Thr Lys Leu Phe Trp Ile Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys Gln Asn Gly Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro Ala Phe Glu Gly Arg Asn Cys Glu Thr His Lys Asp Asp Gln Leu Ile Cys Val Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr Gly Thr Lys Arg Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala Asp Gly Val Ser Cys Thr Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys Pro Gln Gly Arg Ile Val Gly Gly Lys Val Cys Pro Lys Gly Glu Cys Pro Trp Gln Val Leu Leu Val Asn Gly Ala Gln Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg Asn Leu Ile Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly Asp Glu Gln Ser Arg Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr Val Pro Gly Thr Thr Asn His Asp Ile Ala Leu Leu Arg Leu His Gln Pro Val Val Leu Thr Asp His Val Val Pro Leu Cys Leu Pro Glu Arg Thr Phe Ser Glu Arg Thr Leu Ala Phe Val Arg Phe Ser Leu Val Ser Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu Met Val Leu Asn Val Pro Arg Leu Met Thr Gln Asp Cys Leu Gln Gln Ser Arg Lys Val Gly Asp Ser Pro Asn Ile Thr Glu Tyr Met Phe Cys Ala Gly Tyr Ser Asp Gly Ser Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly Pro His Ala Thr His Tyr Arg Gly Thr Trp Tyr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Thr Val Gly His Phe Gly Val Tyr Thr Arg Val Ser Gln Tyr Ile Glu Trp Leu Gln Lys Leu Met Arg Ser Glu Pro Arg Pro Gly Val Leu Leu Arg Ala Pro Phe Pro

FIG. 62A

ATGCAGCGCGTGAACATGATCATGGCAGAATCACCAAGCCTCATCAC CATCTGCCTTTTAGGATATCTACTCAGTGCTGAATGTACAGTTTTTCTT GATCATGAAAACGCCAACAAAATTCTGAATCGGCCAAAGAGGTATAA GTATGGAAGAAAGTGTAGTTTTGAAGAACCACGAGAAGTTTTTGAA AACACTGAAAAGACAACTGAATTTTGGAAGCAGTATGTTGATGGAGA TCAGTGTGAGTCCAATCCATGTTTAAATGGCGGCAGTTGCAAGGATG ACATTAATTCCTATGAATGTTGGTGTCCCTTTGGATTTGAAGGAAAGA ACTGTGAATTAGATGTAACATGTAACATTAAGAATGGCAGATGCGAG CAGTTTTGTAAAAATAGTGCTGATAACAAGGTGGTTTGCTCCTGTACT GAGGGATATCGACTTGCAGAAAACCAGAAGTCCTGTGAACCAGCAGT GCCATTTCCATGTGGAAGAGTTTCTGTTTCACAAACTTCTAAGCTCAC CCGTGCTGAGGCTGTTTTTCCTGATGTGGACTATGTAAATCCTACTGA AGCTGAAACCATTTTGGATAACATCACTCAAGGCACCCAATCATTTA ATGACTTCACTCGGGTTGTTGGTGGAGAAGATGCCAAACCAGGTCAA TTCCCTTGGCAGGTTGTTTTGAATGGTAAAGTTGATGCATTCTGTGGA GGCTCTATCGTTAATGAAAAATGGATTGTAACTGCTGCCCACTGTGTT GAAACTGGTGTTAAAATTACAGTTGTCGCAGGTGAACATAATATTGA GGAGACAGAACATACAGAGCAAAAGCGAAATGTGATTCGAGCAATT ATTCCTCACCACAACTACAATGCAGCTATTAATAAGTACAACCATGA CATTGCCCTTCTGGAACTGGACGAACCCTTAGTGCTAAACAGCTACG TTACACCTATTTGCATTGCTGACAAGGAATACACGAACATCTTCCTCA AATTTGGATCTGGCTATGTAAGTGGCTGGGCAAGAGTCTTCCACAAA GGGAGATCAGCTTTAGTTCTTCAGTACCTTAGAGTTCCACTTGTTGAC CGAGCCACATGTCTTCGATCTACAAAGTTCACCATCTATAACAACAT GTTCTGTGCTGGCTTCCATGAAGGAGGTAGAGATTCATGTCAAGGAG ATAGTGGGGGACCCCATGTTACTGAAGTGGAAGGGACCAGTTTCTTA ACTGGAATTATTAGCTGGGGTGAAGAGTGTGCAATGAAAGGCAAATA TGGAATATACCAAGGTATCCCGGTATGTCAACTGGATTAAGGAAA AAACAAAGCTCACTTAATGAAAGATGGATTTCCAAGGTTAATTCATT **GGAATTGAAAATTAACAG**

FIG. 62B

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Ser Leu Ile Thr Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe LeuAsp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys Met Glu Glu Lys Cys Ser Phe Glu Glu Pro Arg Glu Val Phe Glu Asn Thr Glu Lys Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Ala Val Phe Pro Asp Val Asp Tyr Val Asn Pro Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile Thr Gln Gly Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg Ala Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Ala Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Arg Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr

FIG. 63A

FIG. 63B

Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser Val Phe Leu His Val Leu His Ser Ala Pro Asp Val Gln Asp Cys Pro Glu Cys Thr Leu Gln Glu Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro Ile Leu Gln Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn Val Thr Ser Glu Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr Tyr His Lys Ser

FIG. 63C

FIG. 63D

Met Lys Thr Leu Gln Phe Phe Phe Leu Phe Cys Cys Trp Lys Ala Ile Cys Cys Asn Ser Cys Glu Leu Thr Asn Ile Thr Ile Ala Ile Glu Lys Glu Glu Cys Arg Phe Cys Ile Ser Ile Asn Thr Thr Trp Cys Ala Gly Tyr Cys Tyr Thr Arg Asp Leu Val Tyr Lys Asp Pro Ala Arg Pro Lys Ile Gln Lys Thr Cys Thr Phe Lys Glu Leu Val Tyr Glu Thr Val Arg Val Pro Gly Cys Ala His His Ala Asp Ser Leu Tyr Thr Tyr Pro Val Ala Thr Gln Cys His Cys Gly Lys Cys Asp Ser Asp Ser Thr Asp Cys Thr Val Arg Gly Leu Gly Pro Ser Tyr Cys Ser Phe Gly Glu Met Lys Glu

FIG. 64A

CCCGGAGCCGGGCCACCGCGCCCGCTCTGCTCCGACACCGC GCCCCTGGACAGCCGCCCTCTCCTCCAGGCCCGTGGGGCTGGCCCT GCACCGCCGAGCTTCCCGGGATGAGGGCCCCCGGTGTGGTCACCCGG CGCGCCCAGGTCGCTGAGGGACCCCGGCCAGGCGCGGAGATGGGG GTGCACGAATGTCCTGCCTGGCTGTGGCTTCTCCTGTCCCTGCTGTCG CTCCCTCTGGGCCTCCCAGTCCTGGGCGCCCCACCACGCCTCATCTGT GACAGCCGAGTCCTGGAGAGGTACCTCTTGGAGGCCAAGGAGGCCG AGAATATCACGACGGCTGTGCTGAACACTGCAGCTTGAATGAGAAT ATCACTGTCCCAGACACCAAAGTTAATTTCTATGCCTGGAAGAGGAT GGAGGTCGGCCAGCCGTAGAAGTCTGGCAGGGCCTGGCCCTG CTGTCGGAAGCTGTCCTGCGGGGCCAGGCCCTGTTGGTCAACTCTTCC CAGCCGTGGGAGCCCCTGCAGCTGCATGTGGATAAAGCCGTCAGTGG CCTTCGCAGCCTCACCACTCTGCTTCGGGCTCTGCGAGCCCAGAAGG AAGCCATCTCCCTCCAGATGCGGCCTCAGCTGCTCCACTCCGAACA ATCACTGCTGACACTTTCCGCAAACTCTTCCGAGTCTACTCCAATTTC CTCCGGGGAAAGCTGAAGCTGTACACAGGGGAGGCCTGCAGGACAG GGGACAGATGACCAGGTGTGTCCACCTGGGCATATCCACCACCTCCC TCACCAACATTGCTTGTGCCACACCCTCCCCGCCACTCCTGAACCCC GTCGAGGGCTCTCAGCTCAGCGCCAGCCTGTCCCATGGACACTCCA GTGCCAGCAATGACATCTCAGGGGCCAGAGGAACTGTCCAGAGAGC AACTCTGAGATCTAAGGATGTCACAGGGCCAACTTGAGGGCCCAGAG CAGGAAGCATTCAGAGAGCAGCTTTAAACTCAGGGACAGAGCCATG CTGGGAAGACGCCTGAGCTCACTCGGCACCCTGCAAAATTTGATGCC AGGACACGCTTTGGAGGCGATTTACCTGTTTTCGCACCTACCATCAGG GACAGGATGACCTGGAGAACTTAGGTGGCAAGCTGTGACTTCTCCAG GTCTCACGGGCATGGGCACTCCCTTGGTGGCAAGAGCCCCCTTGACA CCGGGGTGGTGGGAACCATGAAGACAGGATGGGGGCTGGCCTCTGG CTCTCATGGGGTCCAAGTTTTGTGTATTCTTCAACCTCATTGACAAGA ACTGAAACCACCAAAAAAAAAAAAAA

FIG. 64B

Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Arg Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp Arg

FIG. 65

Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp

FIG. 66A

ATGTGGCTGCAGAGCCTGCTGCTCTTTGGGCACTGTGGCCTGCAGCAT CTCTGCACCCGCCCGCTCGCCCAGCCCCAGCACGCAGCCCTGGGAGC ATGTGAATGCCATCCAGGAGGCCCGGCGTCTCCTGAACCTGAGTAGA GACACTGCTGCTGAGATGAATGAAACAGTAGAAGTCATCTCAGAAAT GTTTGACCTCCAGGAGCCGACCTGCCTACAGACCCGCCTGGAGCTGT ACAAGCAGGGCCTGCGGGGCAGCCTCACCAAGCTCAAGGGCCCCTTG ACCATGATGGCCAGCCACTACAAGCAGCACTGCCCTCCAACCCCGGA AACTTCCTGTGCAACCCAGATTATCACCTTTGAAAGTTTCAAAGAGA ACCTGAAGGACTTTCTGCTTGTCATCCCCTTTGACTGCTGGGAGCCAG TCCAGGAGTGA

FIG. 66B

Met Trp Leu Gln Ser Leu Leu Leu Gly Thr Val Ala Cys Ser Ile Ser Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu

FIG. 67A

ATGAAATATACAAGTTATATCTTGGCTTTTCAGCTCTGCATCGTTTTG
GGTTCTCTTGGCTGTTACTGCCAGGACCCATATGTAAAAGAAGCAGA
AAACCTTAAGAAATATTTTAATGCAGGTCATTCAGATGTAGCGGATA
ATGGAACTCTTTTCTTAGGCATTTTGAAGAATTGGAAAGAGGAGAGT
GACAGAAAAATAATGCAGAGCCAAATTGTCTCCTTTTACTTCAAACT
TTTTAAAAACTTTAAAGATGACCAGAGCATCCAAAAGAGTGTGGAGA
CCATCAAGGAAGACATGAATGTCAAGTTTTTCAATAGCAACAAAAAG
AAACGAGATGACTTCGAAAAGCTGACTAATTATTCGGTAACTGACTT
GAATGTCCAACGCAAAGCAATACATGAACTCATCCAAGTGATGGCTG
AACTGTCGCCAGCAGCTAAAACAGGGAAGCGAAAAAAGGAGTCAGAT
GCTGTTTCGAGGTCGAAGAGCATCCCAGTAA

FIG. 67B

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu Gly Ser Leu Gly Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Arg Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg Gly Arg Arg Ala Ser Gln

FIG. 68A

CTGGGACAGTGAATCGACAATGCCGTCTTCTGTCTCGTGGGGCATCCT CCTGCTGGCAGGCCTGTGCTGCCTGGTCCCTGTCTCCCTGGCTGAGGA TCCCCAGGGAGATGCTGCCCAGAAGACAGATACATCCCACCATGATC AGGATCACCCAACCTTCAACAAGATCACCCCCAACCTGGCTGAGTTC GCCTTCAGCCTATACCGCCAGCTGGCACACCAGTCCAACAGCACCAA TATCTTCTCCCCAGTGAGCATCGCTACAGCCTTTGCAATGCTCTC CCTGGGGACCAAGGCTGACACTCACGATGAAATCCTGGAGGCCTGA ATTTCAACCTCACGGAGATTCCGGAGGCTCAGATCCATGAAGGCTTC GACCACCGGCAATGGCCTGTTCCTCAGCGAGGGCCTGAAGCTAGTGG ATAAGTTTTTGGAGGATGTTAAAAAGTTGTACCACTCAGAAGCCTTC ACTGTCAACTTCGGGGACACCGAAGAGGCCAAGAAACAGATCAACG ATTACGTGGAGAAGGGTACTCAAGGGAAAATTGTGGATTTGGTCAAG GAGCTTGACAGAGACACAGTTTTTGCTCTGGTGAATTACATCTTCTTT AAAGGCAAATGGGAGAGACCCTTTGAAGTCAAGGACACCGAGGAAG AGGACTTCCACGTGGACCAGGTGACCACCGTGAAGGTGCCTATGATG AAGCGTTTAGGCATGTTTAACATCCAGCACTGTAAGAAGCTGTCCAG CTGGGTGCTGCTGATGAAATACCTGGGCAATGCCACCGCCATCTTCT TCCTGCCTGATGAGGGGAAACTACAGCACCTGGAAAATGAACTCACC CACGATATCATCACCAAGTTCCTGGAAAATGAAGACAGAAGGTCTGC CAGCTTACATTTACCCAAACTGTCCATTACTGGAACCTATGATCTGAA GAGCGTCCTGGGTCAACTGGGCATCACTAAGGTCTTCAGCAATGGGG CTGACCTCTCCGGGGTCACAGAGGAGGCACCCCTGAAGCTCTCCAAG GCCGTGCATAAGGCTGTGCTGACCATCGACGAGAAAGGGACTGAAGC TGCTGGGGCCATGTTTTTAGAGGCCATACCCATGTCTATCCCCCCCGA GGTCAAGTTCAACAAACCCTTTGTCTTCTTAATGATTGAACAAAATAC AACTGCCTCTCGCTCCTCAACCCCTCCCTCCATCCCTGGCCCCCTCC CTGGATGACATTAAAGAAGGGTTGAGCTGG

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FIG. 68B

Met Pro Ser Ser Val Ser Trp Gly Ile Leu Leu Leu Ala Gly Leu Cys Cys Leu Val Pro Val Ser Leu Ala Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val Phe Ala LeuVal Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu AspArg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr Gln Lys

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GCTAACCTAGTGCCTATAGCTAAGGCAGGTACCTGCATCCTTGTTTTT GTTTAGTGGATCCTCTATCCTTCAGAGACTCTGGAACCCCTGTGGTCT TCTCTTCATCTAATGACCCTGAGGGGATGGAGTTTTCAAGTCCTTCCA AGCCTCACAGGTTTGCTTCTACTTCAGGCAGTGTCGTGGGCATCAGGT GCCCGCCCCTGCATCCCTAAAAGCTTCGGCTACAGCTCGGTGGTGTGT GTCTGCAATGCCACATACTGTGACTCCTTTGACCCCCGACCTTTCCT GCCCTTGGTACCTTCAGCCGCTATGAGAGTACACGCAGTGGGCGACG GATGGAGCTGAGTATGGGGCCCATCCAGGCTAATCACACGGGCACAG GCCTGCTACTGACCCTGCAGCCAGAACAGAAGTTCCAGAAAGTGAAG GGATTTGGAGGGCCATGACAGATGCTGCTGCTCTCAACATCCTTGCC CTGTCACCCCTGCCCAAAATTTGCTACTTAAATCGTACTTCTCTGAA GAAGGAATCGGATATAACATCATCCGGGTACCCATGGCCAGCTGTGA CTTCTCCATCCGCACCTACACCTATGCAGACACCCCTGATGATTTCCA GTTGCACAACTTCAGCCTCCCAGAGGAAGATACCAAGCTCAAGATAC CCCTGATTCACCGAGCCCTGCAGTTGGCCCAGCGTCCCGTTTCACTCC TTGCCAGCCCTGGACATCACCCACTTGGCTCAAGACCAATGGAGCG GTGAATGGGAAGGGTCACTCAAGGGACAGCCCGGAGACATCTACC ACCAGACCTGGGCCAGATACTTTGTGAAGTTCCTGGATGCCTATGCTG AGCACAAGTTACAGTTCTGGGCAGTGACAGCTGAAAATGAGCCTTCT GCTGGGCTGTTGAGTGGATACCCCTTCCAGTGCCTGGGCTTCACCCCT GAACATCAGCGAGACTTCATTGCCCGTGACCTAGGTCCTACCCTCGCC AACAGTACTCACCACAATGTCCGCCTACTCATGCTGGATGACCAACGC TTGCTGCTGCCCCACTGGGCAAAGGTGGTACTGACAGACCCAGAAGC AGCTAAATATGTTCATGGCATTGCTGTACATTGGTACCTGGACTTTCT GGCTCCAGCCAAAGCCACCCTAGGGGAGACACACCGCCTGTTCCCCA ACACCATGCTCTTTGCCTCAGAGGCCTGTGTGGGCTCCAAGTTCTGGG AGCAGAGTGTGCGGCTAGGCTCCTGGGATCGAGGGATGCAGTACAGC CACAGCATCATCACGAACCTCCTGTACCATGTGGTCGGCTGGACCGAC TGGAACCTTGCCCTGAACCCCGAAGGAGGACCCAATTGGGTGCGTAA CTTTGTCGACAGTCCCATCATTGTAGACATCACCAAGGACACGTTTTA CAAACAGCCCATGTTCTACCACCTTGGCCACTTCAGCAAGTTCATTCC TGAGGGCTCCCAGAGAGTGGGGCTGGTTGCCAGTCAGAAGAACGACC TGGACGCAGTGGCACTGATGCATCCCGATGGCTCTGCTGTTGTGGTCG TGCTAAACCGCTCCTCTAAGGATGTGCCTCTTACCATCAAGGATCCTG CTGTGGGCTTCCTGGAGACAATCTCACCTGGCTACTCCATTCACACCT ACCTGTGGCATCGCCAGTGATGGAGCAGATACTCAAGGAGGCACTGG GCTCAGCCTGGGCATTAAAGGGACAGAGTCAGCTCACACGCTGTCTG TGACTAAAGAGGCACAGCAGGGCCAGTGTGAGCTTACAGCGACGT

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FIG. 69A-2

FIG. 69B

Met Glu Phe Ser Ser Pro Ser Arg Glu Glu Cys Pro Lys Pro Leu Ser Arg Val Ser Ile Met Ala Gly Ser Leu Thr Gly Leu Leu Leu Leu Gln Ala Val Ser Trp Ala Ser Gly Ala Arg Pro Cys Ile Pro Lys Ser Phe Gly Tyr Ser Ser Val Val Cys Val Cys Asn Ala Thr Tyr Cys Asp Ser Phe Asp Pro Pro Thr Phe Pro Ala Leu Gly Thr Phe Ser Arg Tyr Glu Ser Thr Arg Ser Gly Arg Arg Met Glu Leu Ser Met Gly Pro Ile Gln Ala Asn His Thr Gly Thr Gly Leu Leu Leu Thr Leu Gln Pro Glu Gln Lys Phe Gln Lys Val Lys Gly Phe Gly Gly Ala Met Thr Asp Ala Ala Ala Leu Asn Ile Leu Ala Leu Ser Pro Pro Ala Gln Asn Leu Leu Leu Lys Ser Tyr Phe Ser Glu Glu Gly Ile Gly Tyr Asn Ile Ile Arg Val Pro Met Ala Ser Cys Asp Phe Ser Ile Arg Thr Tyr Thr Tyr Ala Asp Thr Pro Asp Asp Phe Gln Leu His Asn Phe Ser Leu Pro Glu Glu Asp Thr Lys Leu Lys Ile Pro Leu Ile His Arg Ala Leu Gln Leu Ala Gln Arg Pro Val Ser Leu Leu Ala Ser Pro Trp Thr Ser Pro Thr Trp Leu Lys Thr Asn Gly Ala Val Asn Gly Lys Gly Ser Leu Lys Gly Gln Pro Gly Asp Ile Tyr His Gln Thr Trp Ala Arg Tyr Phe Val Lys Phe Leu Asp Ala Tyr Ala Glu His Lys Leu Gln Phe Trp Ala Val Thr Ala Glu Asn Glu Pro Ser Ala Gly Leu Leu Ser Gly Tyr Pro Phe Gln Cys Leu Gly Phe Thr Pro Glu His Gln Arg Asp Phe Ile Ala Arg Asp Leu Gly Pro Thr Leu Ala Asn Ser Thr His His Asn Val Arg Leu Leu Met Leu Asp Asp Gln Arg Leu Leu Leu Pro His Trp Ala Lys Val Val Leu Thr Asp Pro Glu Ala Ala Lys Tyr Val His Gly Ile Ala Val His Trp Tyr Leu Asp Phe Leu Ala Pro Ala Lys Ala Thr Leu Gly Glu Thr His Arg Leu Phe Pro Asn Thr Met Leu Phe Ala Ser Glu Ala Cys Val Gly Ser Lys Phe Trp Glu Gln Ser Val Arg Leu Gly Ser Trp Asp Arg Gly Met Gln Tyr Ser His Ser Ile Île Thr Asn Leu Leu Tyr His Val Val Gly Trp Thr Asp Trp Asn Leu Ala Leu Asn Pro Glu Gly Gly Pro Asn Trp Val Arg Asn Phe Val Asp Ser Pro Ile Ile Val Asp Ile Thr Lys Asp Thr Phe Tyr Lys Gln Pro Met Phe Tyr His Leu Gly His Phe Ser Lys Phe Ile Pro Glu Gly Ser Gln Arg Val Gly Leu Val Ala Ser Gln Lys Asn Asp Leu Asp Ala Val Ala Leu Met His Pro Asp Gly Ser Ala Val Val Val Val Leu Asn Arg Ser Ser Lys Asp Val Pro Leu Thr Ile Lys Asp Pro Ala Val Gly Phe Leu Glu Thr Ile Ser Pro Gly Tyr Ser Ile His Thr Tyr Leu Trp His Arg Gln

FIG. 70A

ATGGATGCAATGAAGAGAGGGCTCTGCTGTGTGCTGCTGTGTGG AGCAGTCTTCGTTTCGCCCAGCCAGGAAATCCATGCCCGATTCAGAA GAGGAGCCAGATCTTACCAAGTGATCTGCAGAGATGAAAAAACGCA GATGATATACCAGCAACATCAGTCATGGCTGCGCCCTGTGCTCAGAA GCAACCGGGTGGAATATTGCTGGTGCAACAGTGGCAGGGCACAGTGC CACTCAGTGCCTGTCAAAAGTTGCAGCGAGCCAAGGTGTTTCAACGG GGGCACCTGCCAGCAGGCCCTGTACTTCTCAGATTTCGTGTGCCAGTG CCCGAAGGATTTGCTGGGAAGTGCTGTGAAATAGATACCAGGGCCA CGTGCTACGAGGACCAGGGCATCAGCTACAGGGGCACGTGGAGCAC AGCGGAGAGTGGCGCGAGTGCACCAACTGGAACAGCAGCGCGTTG GCCCAGAAGCCCTACAGCGGGCGGAGGCCAGACGCCATCAGGCTGG GCCTGGGGAACCACAACTACTGCAGAAACCCAGATCGAGACTCAAA GCCCTGGTGCTACGTCTTTAAGGCGGGGAAGTACAGCTCAGAGTTCT GCAGCACCCCTGCCTGCTCTGAGGGAAACAGTGACTGCTACTTTGGG AATGGGTCAGCCTACCGTGGCACGCACAGCCTCACCGAGTCGGGTGC CTCCTGCCTCCGTGGAATTCCATGATCCTGATAGGCAAGGTTTACAC AGCACAGAACCCCAGTGCCCAGGCACTGGGCCTGGGCAAACATAATT ACTGCCGGAATCCTGATGGGGATGCCAAGCCCTGGTGCCACGTGCTG AAGAACCGCAGGCTGACGTGGGAGTACTGTGATGTGCCCTCCTGCTC CACCTGCGGCCTGAGACAGTACAGCCAGCCTCAGTTTCGCATCAAAG GAGGGCTCTTCGCCGACATCGCCTCCCACCCCTGGCAGGCTGCCATCT TTGCCAAGCACAGGAGGTCGCCGGGAGAGCGGTTCCTGTGCGGGGGC ATACTCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCACTGCTTCCAG GAGAGGTTTCCGCCCCACCACCTGACGGTGATCTTGGGCAGAACATA CCGGGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGAAAAA TACATTGTCCATAAGGAATTCGATGATGACACTTACGACAATGACAT TGCGCTGCTGCAGCTGAAATCGGATTCGTCCCGCTGTGCCCAGGAGA GCAGCGTGGTCCGCACTGTGTGCCTTCCCCCGGCGGACCTGCAGCTG CCGGACTGGACGGAGTGTGAGCTCTCCGGCTACGGCAAGCATGAGGC CTTGTCTCCTTTCTATTCGGAGCGGCTGAAGGAGGCTCATGTCAGACT GTACCCATCCAGCCGCTGCACATCACAACATTTACTTAACAGAACAG TCACCGACAACATGCTGTGTGCTGGAGACACTCGGAGCGGCGGCCC CAGGCAAACTTGCACGACGCCTGCCAGGGCGATTCGGGAGGCCCCCT GGTGTGTCTGAACGATGGCCGCATGACTTTGGTGGGCATCATCAGCT GGGGCCTGGGCTGTGGACAGAAGGATGTCCCGGGTGTGTACACCAAG GTTACCAACTACCTAGACTGGATTCGTGACAACATGCGACCGTGACC AGGAACACCCGACTCCTCAAAAGCAAATGAGATCC

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FIG. 70B

Met Asp Ala Met Lys Arg Gly Leu Cys Cys Val Leu Leu Leu Cys Gly Ala Val Phe Val Ser Pro Ser Gln Glu Ile His Ala Arg Phe Arg Arg Gly Ala Arg Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro

FIG. 71A

ATCACTCTCTTTAATCACTACTCACATTAACCTCAACTCCTGCCACAA TGTACAGGATGCAACTCCTGTCTTGCATTGCACTAATTCTTGCACTTG TCACAAACAGTGCACCTACTTCAAGTTCGACAAAGAAAACAAAGAAA ACACAGCTACAACTGGAGCATTTACTGCTGGATTTACAGATGATTTTG AATGGAATTAATAATTACAAGAATCCCAAACTCACCAGGATGCTCAC ATTTAAGTTTTACATGCCCAAGAAGGCCACAGAACTGAAACAGCTTC AGTGTCTAGAAGAAGAACTCAAACCTCTGGAGGAAGTGCTGAATTTA GCTCAAAGCAAAAACTTTCACTTAAGACCCAGGGACTTAATCAGCAA TATCAACGTAATAGTTCTGGAACTAAAGGGATCTGAAACAACATTCA TGTGTGAATATGCAGATGAGACAGCAACCATTGTAGAATTTCTGAAC AGATGGATTACCTTTTGTCAAAGCATCATCTCAACACTAACTTGATAA AATATTTAAATTTTATTTGTTGAATGTATGGTTGCTACCTATTG TAACTATTATTCTTAATCTTAAAACTATAAATATGGATCTTTTATGAT CAAAAATATTTATTATTGTTGAATGTTAAATATAGTATCTATGTAG AAACAAAAAAAAAA

FIG. 71B

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ile Leu Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys Gln Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr

FIG. 72A-1

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ATGCAAATAGAGCTCTCCACCTGCTTCTTTCTGTGCCTTTTTGCGATTCT GCTTTAGTGCCACCAGAAGATACTACCTGGGTGCAGTGGAACTGTCA TGGGACTATATGCAAAGTGATCTCGGTGAGCTGCCTGTGGACGCAAG ATTTCCTCCTAGAGTGCCAAAATCTTTTCCATTCAACACCTCAGTCGT GTACAAAAAGACTCTGTTTGTAGAATTCACGGATCACCTTTTCAACAT CGCTAAGCCAAGGCCACCCTGGATGGGTCTGCTAGGTCCTACCATCC AGGCTGAGGTTTATGATACAGTGGTCATTACACTTAAGAACATGGCT TCCCATCCTGTCAGTCTTCATGCTGTTGTGTGTATCCTACTGGAAAGCT TCTGAGGGAGCTGAATATGATGATCAGACCAGTCAAAGGGAGAAAG AAGATGATAAAGTCTTCCCTGGTGGAAGCCATACATATGTCTGGCAG GTCCTGAAAGAGAATGGTCCAATGGCCTCTGACCCACTGTGCCTTAC CTACTCATATCTTCTCATGTGGACCTGGTAAAAGACTTGAATTCAGG CCTCATTGGAGCCCTACTAGTATGTAGAGAAGGGAGTCTGGCCAAGG AAAAGACACAGACCTTGCACAAATTTATACTACTTTTTGCTGTATTTG ATGAAGGGAAAAGTTGGCACTCAGAAACAAAGAACTCCTTGATGCA GGATAGGGATGCTGCATCTGCTCGGGCCTAAAATGCACACAG TCAATGGTTATGTAAACAGGTCTCTGCCAGGTCTGATTGGATGCCACA GGAAATCAGTCTATTGGCATGTGATTGGAATGGGCACCACTCCTGAA GTGCACTCAATATTCCTCGAAGGTCACACATTTCTTGTGAGGAACCAT CGCCAGGCGTCCTTGGAAATCTCGCCAATAACTTTCCTTACTGCTCAA ACACTCTTGATGGACCTTGGACAGTTTCTACTGTTTTGTCATATCTCTT CCCACCAACATGATGGCATGGAAGCTTATGTCAAAGTAGACAGCTGT CCAGAGGAACCCCAACTACGAATGAAAAATAATGAAGAAGCGGAAG ACTATGATGATGATCTTACTGATTCTGAAATGGATGTGGTCAGGTTTG ATGATGACAACTCTCCTTCCTTTATCCAAATTCGCTCAGTTGCCAAGA AGCATCCTAAAACTTGGGTACATTACATTGCTGCTGAAGAGGAGGAC TGGGACTATGCTCCCTTAGTCCTCGCCCCCGATGACAGAAGTTATAAA AGTCAATATTTGAACAATGGCCCTCAGCGGATTGGTAGGAAGTACAA AAAAGTCCGATTTATGGCATACACAGATGAAACCTTTAAGACTCGTG AAGCTATTCAGCATGAATCAGGAATCTTGGGACCTTTACTTTATGGGG TCAAGGAGATTACCAAAAGGTGTAAAACATTTGAAGGATTTTCCAAT TCTGCCAGGAGAAATATTCAAATATAAATGGACAGTGACTGTAGAAG ATGGGCCAACTAAATCAGATCCTCGGTGCCTGACCCGCTATTACTCTA GTTTCGTTAATATGGAGAGAGATCTAGCTTCAGGACTCATTGGCCCTC TCCTCATCTGCTACAAAGAATCTGTAGATCAAAGAGGAAACCAGATA ATGTCAGACAAGAGGAATGTCATCCTGTTTTCTGTATTTGATGAGAAC CGAAGCTGGTACCTCACAGAGAATATACAACGCTTTCTCCCCAATCCA GCTGGAGTGCAGCTTGAGGATCCAGAGTTCCAAGCCTCCAACATCAT GCACAGCATCAATGGCTATGTTTTTGATAGTTTGCAGTTTGCAGTTTTG TTTGCATGAGGTGGCATACTGGTACATTCTAAGCATTGGAGCACAGA CTGACTTCCTTCTCTCTCTCTGGATATACCTTCAAACACAAAAT

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FIG. 72A-2

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GGTCTATGAAGACACACTCACCCTATTCCCATTCTCAGGAGAAACTGT CTTCATGTCGATGGAAAACCCAGGTCTATGGATTCTGGGGTGCCACA ACTCAGACTTTCGGAACAGAGGCATGACCGCCTTACTGAAGGTTTCT AGTTGTGACAAGAACACTGGTGATTATTACGAGGACAGTTATGAAGA TATTTCAGCATACTTGCTGAGTAAAAACAATGCCATTGAACCAAGAA GCTTCTCCCAGAATTCAAGACACCGTAGCACTAGGCAAAAGCAATTT AATGCCACCACAATTCCAGAAAATGACATAGAGAAGACTGACCCTTG GTTTGCACACAGAACACCTATGCCTAAAATACAAAATGTCTCCTCTA GTGATTTGTTGATGCTCTTGCGACAGAGTCCTACTCCACATGGGCTAT CCTTATCTGATCTCCAAGAAGCCAAATATGAGACTTTTTCTGATGATC CATCACCTGGAGCAATAGACAGTAATAACAGCCTGTCTGAAATGACA CACTTCAGGCCACAGCTCCATCACAGTGGGGACATGGTATTTACCCC TGAGTCAGGCCTCCAATTAAGATTAAATGAGAAACTGGGGACAACTG CAGCAACAGAGTTGAAGAAACTTGATTTCAAAGTTTCTAGTACATCA AATAATCTGATTTCAACAATTCCATCAGACAATTTGGCAGCAGGTACT GATAATACAAGTTCCTTAGGACCCCCAAGTATGCCAGTTCATTATGAT AGTCAATTAGATACCACTCTATTTGGCAAAAAGTCATCTCCCCTTACT GAGTCTGGTGGACCTCTGAGCTTGAGTGAAGAAAATAATGATTCAAA GTTGTTAGAATCAGGTTTAATGAATAGCCAAGAAAGTTCATGGGGAA AAAATGTATCGTCAACAGAGAGTGGTAGGTTATTTAAAGGGAAAAGA GCTCATGGACCTGCTTTGTTGACTAAAGATAATGCCTTATTCAAAGTT AGCATCTCTTTGTTAAAGACAAACAAAACTTCCAATAATTCAGCAACT AATAGAAAGACTCACATTGATGGCCCATCATTATTAATTGAGAATAG TCCATCAGTCTGGCAAAATATATTAGAAAGTGACACTGAGTTTAAAA AAGTGACACCTTTGATTCATGACAGAATGCTTATGGACAAAAATGCT ACAGCTTTGAGGCTAAATCATATGTCAAATAAAACTACTTCATCAAA AAACATGGAAATGGTCCAACAGAAAAAAGAGGGCCCCATTCCACCA GATGCACAAAATCCAGATATGTCGTTCTTTAAGATGCTATTCTTGCCA GAATCAGCAAGGTGGATACAAAGGACTCATGGAAAGAACTCTCTGAA CTCTGGGCAAGGCCCCAGTCCAAAGCAATTAGTATCCTTAGGACCAG AAAAATCTGTGGAAGGTCAGAATTTCTTGTCTGAGAAAAACAAAGTG GTAGTAGGAAAGGGTGAATTTACAAAGGACGTAGGACTCAAAGAGA TGGTTTTTCCAAGCAGCAGAAACCTATTTCTTACTAACTTGGATAATT TACATGAAAATAATACACACAATCAAGAAAAAAAAAATTCAGGAAGA AATAGAAAAGAAGGAAACATTAATCCAAGAGAATGTAGTTTTGCCTC AGATACATACAGTGACTGGCACTAAGAATTTCATGAAGAACCTTTTC TTACTGAGCACTAGGCAAAATGTAGAAGGTTCATATGACGGGGCATA TGCTCCAGTACTTCAAGATTTTAGGTCATTAAATGATTCAACAAATAG AACAAAGAAACACACAGCTCATTTCTCAAAAAAAGGGGAGGAAGAA AACTTGGAAGGCTTGGGAAATCAAACCAGCAAATTGTAGAGAAATAT GCATGCACCACAAGGAATATCTCCTAATACAAGCCAGCAGAATTTTG TCACGCAACGTAGTAAGAGAGCTTTGAAACAATTCAGACTCCCACTA FIG. 72A-3

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GAAGAACAGAACTTGAAAAAAGGATAATTGTGGATGACACCTCAAC CCAGTGGTCCAAAAACATGAAACATTTGACCCCGAGCACCCTCACAC AGATAGACTACAATGAGAAGGAGAAAGGGGCCATTACTCAGTCTCCC TTATCAGATTGCCTTACGAGGAGTCATAGCATCCCTCAAGCAAATAGA TCTCCATTACCCATTGCAAAGGTATCATCATCTATTAGACCTA TATATCTGACCAGGGTCCTATTCCAAGACAACTCTTCTCATCTTCCAG CAGCATCTTATAGAAAGAAAGATTCTGGGGTCCAAGAAAGCAGTCAT TTCTTACAAGGAGCCAAAAAAAAAAAACCTTTCTTTAGCCATTCTAACC TTGGAGATGACTGGTGATCAAAGAGAGGTTGGCTCCCTGGGGACAAG TGCCACAAATTCAGTCACATACAAGAAAGTTGAGAACACTGTTCTCCC GAAACCAGACTTGCCCAAAACATCTGGCAAAGTTGAATTGCTTCCAA AAGTTCACATTTATCAGAAGGACCTATTCCCTACGGAAACTAGCAATG GGTCTCCTGGCCATCTGGATCTCGTGGAAGGGAGCCTTCTTCAGGGAA CAGAGGGAGCGATTAAGTGGAATGAAGCAAACAGACCTGGAAAAGT GCTATTGGATCCTCTTGCTTGGGATAACCACTATGGTACTCAGATACC AAAAGAAGAGTGGAAATCCCAAGAGAAGTCACCAGAAAAAACAGCT TTTAAGAAAAAGGATACCATTTTGTCCCTGAACGCTTGTGAAAGCAAT CATGCAATAGCAGCAATAAATGAGGGACAAAATAAGCCCGAAATAG AAGTCACCTGGGCAAAGCAAGGTAGGACTGAAAGGCTGTGCTCTCAA AACCCACCAGTCTTGAAACGCCATCAACGGGAAATAACTCGTACTAC TCTTCAGTCAGATCAAGAGGAAATTGACTATGATGATACCATATCAGT TGAAATGAAGAAGGAAGATTTTGACATTTATGATGAGGATGAAAATC AGAGCCCCCGCAGCTTTCAAAAGAAAACACGACACTATTTTATTGCTG CAGTGGAGAGGCTCTGGGATTATGGGATGAGTAGCTCCCCACATGTT CTAAGAAACAGGGCTCAGAGTGGCAGTGTCCCTCAGTTCAAGAAAGT TGTTTTCCAGGAATTTACTGATGGCTCCTTTACTCAGCCCTTATACCGT GGAGAACTAAATGAACATTTGGGACTCCTGGGGCCATATATAAGAGC AGAAGTTGAAGATAATATCATGGTAACTTTCAGAAATCAGGCCTCTC GTCCCTATTCCTATTCTAGCCTTATTTCTTATGAGGAAGATCAGAG GCAAGGAGCAGAACCTAGAAAAACTTTGTCAAGCCTAATGAAACCA AAACTTACTTTTGGAAAGTGCAACATCATATGGCACCCACTAAAGAT GAGTTTGACTGCAAAGCCTGGGCTTATTTCTCTGATGTTGACCTGGAA AAAGATGTGCACTCAGGCCTGATTGGACCCCTTCTGGTCTGCCACACT AACACACTGAACCCTGCTCATGGGAGACAAGTGACAGTACAGGAATT TGCTCTGTTTTCACCATCTTTGATGAGACCAAAAGCTGGTACTTCACT GAAAATATGGAAAGAAACTGCAGGGCTCCCTGCAATATCCAGATGGA CATAATGGATACACTACCTGGCTTAGTAATGGCTCAGGATCAAAGGA TTCGATGGTATCTGCTCAGCATGGGCAGCAATGAAAACATCCATTCT ATTCATTTCAGTGGACATGTGTTCACTGTACGAAAAAAAGAGGAGTA TAAAATGGCACTGTACAATCTCTATCCAGGTGTTTTTTGAGACAGTGGA

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FIG. 72A-4

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AATGTTACCATCCAAAGCTGGAATTTGGCGGGTGGAATGCCTTATTGG CGAGCATCTACATGCTGGGATGAGCACACTTTTTCTGGTGTACAGCAA TAAGTGTCAGACTCCCCTGGGAATGGCTTCTGGACACATTAGAGATTT TCAGATTACAGCTTCAGGACAATATGGACAGTGGGCCCCAAAGCTGG CCAGACTTCATTATTCCGGATCAATCAATGCCTGGAGCACCAAGGAG CCCTTTTCTTGGATCAAGGTGGATCTGTTGGCACCAATGATTATTCAC GGCATCAAGACCCAGGGTGCCCGTCAGAAGTTCTCCAGCCTCTACAT CTCTCAGTTTATCATCATGTATAGTCTTGATGGGAAGAAGTGGCAGA CTTATCGAGGAAATTCCACTGGAACCTTAATGGTCTTCTTTGGCAATG TGGATTCATCTGGGATAAAACACAATATTTTTAACCCTCCAATTATTG CTCGATACATCCGTTTGCACCCAACTCATTATAGCATTCGCAGCACTC TTCGCATGGAGTTGATGGGCTGTGATTTAAATAGTTGCAGCATGCCAT TGGGAATGGAGAGTAAAGCAATATCAGATGCACAGATTACTGCTTCA TCCTACTTTACCAATATGTTTGCCACCTGGTCTCCTTCAAAAGCTCGA CTTCACCTCCAAGGGAGGAGTAATGCCTGGAGACCTCAGGTGAATAA TCCAAAAGAGTGGCTGCAAGTGGACTTCCAGAAGACAATGAAAGTCA CAGGAGTAACTACTCAGGGAGTAAAATCTCTGCTTACCAGCATGTAT GTGAAGGAGTTCCTCATCTCCAGCAGTCAAGATGGCCATCAGTGGAC TCTCTTTTTCAGAATGGCAAAGTAAAGGTTTTTCAGGGAAATCAAGA CTCCTTCACACCTGTGGTGAACTCTCTAGACCCACCGTTACTGACTCG CTACCTTCGAATTCACCCCCAGAGTTGGGTGCACCAGATTGCCCTGAG GATGGAGGTTCTGGGCTGCGAGGCACAGGACCTCTACTGAGGGTGGC CACTGCAGCACCTGCCACTGCCGTCACCTCTCCTCAGCTCCAGG GCAGTGTCCCTCCCTGGCTTGCCTTCTACCTTTGTGCTAAATCCTAGC AGACACTGCCTTGAAGCCTCCTGAATTAACTATCATCAGTCCTGCATT TCTTTGGTGGGGGCCAGGAGGGTGCATCCAATTTAACTTAACTCTTA CCTATTTCTGCAGCTGCTCCCAGATTACTCCTTCCTTCCAATATAACT AGGCAAAAAGAAGTGAGGAGAAACCTGCATGAAAGCATTCTTCCCTG AAAAGTTAGGCCTCTCAGAGTCACCACTTCCTCTGTTGTAGAAAAACT ATGTGATGAAACTTTGAAAAAGATATTTATGATGTTAACATTTCAGGT TAAGCCTCATACGTTTAAAATAAAACTCTCAGTTGTTTATTATCCTGA TCAAGCATGGAACAAAGCATGTTTCAGGATCAGATCAATACAATCTT GGAGTCAAAAGGCAAATCATTTGGACAATCTGCAAAATGGAGAGAA TACAATAACTACTACAGTAAAGTCTGTTTCTGCTTCCTTACACATAGA TATAATTATGTTATTTAGTCATTATGAGGGGCACATTCTTATCTCCAA AACTAGCATTCTTAAACTGAGAATTATAGATGGGGTTCAAGAATCCC TAAGTCCCCTGAAATTATATAAGGCATTCTGTATAAATGCAAATGTGC ATTTTTCTGACGAGTGTCCATAGATATAAAGCCATTTGGTCTTAATTCT GACCAATAAAAAAATAAGTCAGGAGGATGCAATTGTTGAAAGCTTTG AAATGATGA

FIG. 72B-1

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe Cys Phe Ser Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gin Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Île Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe

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FIG. 72B-2

Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Arg Ser Thr Arg Gln Lys Gln Phe Asn Ala Thr Thr Ile Pro Glu Asn Asp Ile Glu Lys Thr Asp Pro Trp Phe Ala His Arg Thr Pro Met Pro Lys Ile Gln Asn Val Ser Ser Ser Asp Leu Leu Met Leu Leu Arg Gln Ser Pro Thr Pro His Gly Leu Ser Leu Ser Asp Leu Gln Glu Ala Lys Tyr Glu Thr Phe Ser Asp Asp Pro Ser Pro Gly Ala Ile Asp Ser Asn Asn Ser Leu Ser Glu Met Thr His Phe Arg Pro Gln Leu His His Ser Gly Asp Met Val Phe Thr Pro Glu Ser Gly Leu Gln Leu Arg Leu Asn Glu Lys Leu Gly Thr Thr Ala Ala Thr Glu Leu Lys Lys Leu Asp Phe Lys Val Ser Ser Thr Ser Asn Asn Leu Ile Ser Thr Ile Pro Ser Asp Asn Leu Ala Ala Gly Thr Asp Asn Thr Ser Ser Leu Gly Pro Pro Ser Met Pro Val His Tyr Asp Ser Gln Leu Asp Thr Thr Leu Phe Gly Lys Lys Ser Ser Pro Leu Thr Glu Ser Gly Gly Pro Leu Ser Leu Ser Glu Glu Asn Asn Asp Ser Lys Leu Leu Glu Ser Gly Leu Met Asn Ser Gln Glu Ser Ser Trp Gly Lys Asn Val Ser Ser Thr Glu Ser Gly Arg Leu Phe Lys Gly Lys Arg Ala His Gly Pro Ala Leu Leu Thr Lys Asp Asn Ala Leu Phe Lys Val Ser Ile Ser Leu Leu Lys Thr Asn Lys Thr Ser Asn Asn Ser Ala Thr Asn Arg Lys Thr His Ile Asp Gly Pro Ser Leu Leu Ile Glu Asn Ser Pro Ser Val Trp Gln Asn Ile Leu Glu Ser Asp Thr Glu Phe Lys Lys Val Thr Pro Leu Ile His Asp Arg Met Leu Met Asp Lys Asn Ala Thr Ala Leu Arg Leu Asn His Met Ser Asn Lys Thr Thr Ser Ser Lys Asn Met Glu Met Val Gln Gln Lys Lys Glu Gly Pro Ile Pro Pro Asp Ala Gln Asn Pro Asp Met Ser Phe Phe Lys Met Leu Phe Leu Pro Glu Ser Ala Arg Trp Ile Gln Arg Thr His Gly Lys Asn Ser Leu Asn Ser Gly Gln Gly Pro Ser Pro Lys Gln Leu Val Ser Leu Gly Pro Glu Lys Ser Val Glu Gly Gln Asn Phe Leu Ser Glu Lys Asn Lys Val Val Val Gly Lys Gly Glu Phe Thr Lys Asp Val Gly Leu Lys Glu Met Val Phe Pro Ser Ser Arg Asn Leu Phe Leu Thr Asn Leu Asp Asn Leu His Glu Asn Asn Thr His Asn Gln Glu Lys Lys Ile Gln Glu Glu Ile Glu Lys Lys Glu Thr Leu Ile Gln Glu Asn Val Val Leu Pro Gln Ile His Thr Val Thr Gly Thr Lys Asn Phe Met Lys Asn Leu Phe Leu Leu Ser Thr Arg Gln Asn Val Glu Gly Ser Tyr Asp Gly Ala Tyr Ala Pro Val Leu Gln Asp Phe Arg Ser Leu Asn Asp Ser Thr Asn Arg Thr Lys Lys His Thr Ala His Phe Ser Lys Lys Gly Glu Glu Glu Asn Leu Glu Gly Leu Gly Asn Gln Thr Lys Gln Ile Val Glu Lys Tyr Ala Cys Thr Thr Arg Ile Ser Pro Asn Thr Ser Gln Gln Asn Phe Val Thr Gln Arg Ser Lys Arg Ala Leu Lys Gln Phe Arg Leu Pro Leu Glu Glu Thr Glu Leu Glu Lys Arg Ile Ile Val Asp Asp Thr Ser Thr Gln Trp Ser Lys Asn Met Lys His Leu Thr Pro Ser Thr Leu Thr Gln Ile Asp Tyr Asn Glu Lys Glu Lys Gly Ala Ile Thr Gln Ser Pro Leu Ser Asp Cys Leu Thr Arg Ser His Ser Ile Pro Gln Ala Asn Arg Ser Pro Leu Pro Ile Ala Lys Val Ser Ser Phe Pro Ser Ile Arg Pro Ile Tyr Leu Thr Arg Val Leu Phe Gln Asp Asn Ser Ser His Leu Pro

FIG. 72B-3

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Ala Ala Ser Tyr Arg Lys Lys Asp Ser Gly Val Gln Glu Ser Ser His Phe Leu Gln Gly Ala Lys Lys Asn Asn Leu Ser Leu Ala Ile Leu Thr Leu Glu Met Thr Gly Asp Gln Arg Glu Val Gly Ser Leu Gly Thr Ser Ala Thr Asn Ser Val Thr Tyr Lys Lys Val Glu Asn Thr Val Leu Pro Lys Pro Asp Leu Pro Lys Thr Ser Gly Lys Val Glu Leu Leu Pro Lys Val His Ile Tyr Gln Lys Asp Leu Phe Pro Thr Glu Thr Ser Asn Gly Ser Pro Gly His Leu Asp Leu Val Glu Gly Ser Leu Leu Gln Gly Thr Glu Gly Ala Ile Lys Trp Asn Glu Ala Asn Arg Pro Gly Lys Val Pro Phe Leu Arg Val Ala Thr Glu Ser Ser Ala Lys Thr Pro Ser Lys Leu Leu Asp Pro Leu Ala Trp Asp Asn His Tyr Gly Thr Gln Ile Pro Lys Glu Glu Trp Lys Ser Gln Glu Lys Ser Pro Glu Lys Thr Ala Phe Lys Lys Asp Thr Ile Leu Ser Leu Asn Ala Cys Glu Ser Asn His Ala Ile Ala Ile Asn Glu Gly Gln Asn Lys Pro Glu Ile Glu Val Thr Trp Ala Lys Gln Gly Arg Thr Glu Arg Leu Cys Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp Glu As Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys Arg Ala Pro Cys Asn Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe Thr Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile Trp Arg Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg Asp Phe Gin Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn Val Asp Ser Ser Gly Ile

FIG. 72B-4

Lys His Asn Ile Phe Asn Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr

FIG. 73A

TCCACCTGTCCCGCAGCGCCGGCTCGCGCCCTCCTGCCGCAGCCACC GAGCCGCCGTCTAGCGCCCCGACCTCGCCACCATGAGAGCCCTGCTG GCGCGCCTGCTTCTCTGCGTCCTGGTCGTGAGCGACTCCAAAGGCAGC AATGAACTTCATCAAGTTCCATCGAACTGTGACTGTCTAAATGGAGGA ACATGTGTGTCCAACAAGTACTTCTCCAACATTCACTGGTGCAACTGC CCAAAGAAATTCGGAGGGCAGCACTGTGAAATAGATAAGTCAAAAAC CTGCTATGAGGGGAATGGTCACTTTTACCGAGGAAAGGCCAGCACTG ACACCATGGGCCGGCCCTGCCTGGAACTCTGCCACTGTCCTTC AGCAAACGTACCATGCCCACAGATCTGATGCTCTTCAGCTGGGCCTGG GGAAACATAATTACTGCAGGAACCCAGACAACCGGAGGCGACCCTGG TGCTATGTGCAGGTGGGCCTAAAGCCGCTTGTCCAAGAGTGCATGGT GCATGACTGCGCAGATGGAAAAAAGCCCTCCTCTCCTCCAGAAGAAT TAAAATTTCAGTGTGGCCAAAAGACTCTGAGGCCCCGCTTTAAGATTA TTGGGGGAGAATTCACCACCATCGAGAACCAGCCCTGGTTTGCGGCC ATCTACAGGAGGCACCGGGGGGGCTCTGTCACCTACGTGTGTGGAGG CAGCCTCATCAGCCCTTGCTGGGTGATCAGCGCCACACACTGCTTCAT TGATTACCCAAAGAAGGAGGACTACATCGTCTACCTGGGTCGCTCAA GGCTTAACTCCAACACGCAAGGGGAGATGAAGTTTGAGGTGGAAAAC CTCATCCTACACAAGGACTACAGCGCTGACACGCTTGCTCACCACAAC GACATTGCCTTGCAAGATCCGTTCCAAGGAGGCAGGTGTGCGCA GCCATCCCGGACTATACAGACCATCTGCCTGCCCTCGATGTATAACGA TCCCCAGTTTGGCACAAGCTGTGAGATCACTGGCTTTGGAAAAGAGA ATTCTACCGACTATCTCTATCCGGAGCAGCTGAAGATGACTGTTGTGA AGCTGATTTCCCACCGGGAGTGTCAGCAGCCCCACTACTACGGCTCTG AAGTCACCACAAAATGCTGTGTGCTGCTGACCCACAGTGGAAAACA GATTCCTGCCAGGGAGACTCAGGGGGACCCCTCGTCTGTTCCCTCCAA GGCCGCATGACTTTGACTGGAATTGTGAGCTGGGGCCGTGGATGTGC CCTGAAGGACAAGCCAGGCGTCTACACGAGAGTCTCACACTTCTTAC CCTGGATCCGCAGTCACACCAAGGAAGAGAATGGCCTGGCCCTCTGA GGGTCCCCAGGGAGAAACGGGCACCACCCGCTTTCTTGCTGGTTGTC ATTTTTGCAGTAGAGTCATCTCCATCAGCTGTAAGAAGAGACTGGGA AGAT

FIG. 73B

Met Arg Ala Leu Leu Ala Arg Leu Leu Leu Cys Val Leu Val Val Ser Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg Phe Lys Ile Ile Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

FIG.74A

TCCTGCACAGGCAGTGCCTTGAAGTGCTTCTTCAGAGACCTTTCTTCA TAGACTACTTTTTTTTTTTAAGCAGCAAAAGGAGAAAATTGTCATCA AGGATATTCCAGATTCTTGACAGCATTCTCGTCATCTCTGAGGACATC ACCATCATCTCAGGATGAGGGGCATGAAGCTGCTGGGGGGCGCTGCTG GCACTGGCGGCCCTACTGCAGGGGGCCGTGTCCCTGAAGATCGCAGC CTTCAACATCCAGACATTTGGGGAGACCAAGATGTCCAATGCCACCCT CGTCAGCTACATTGTGCAGATCCTGAGCCGCTATGACATCGCCCTGGT CCAGGAGGTCAGAGACAGCCACCTGACTGCCGTGGGGAAGCTGCTGG ACAACCTCAATCAGGATGCACCAGACACCTATCACTACGTGGTCAGT GAGCCACTGGGACGGAACAGCTATAAGGAGCGCTACCTGTTCGTGTA CAGGCCTGACCAGGTGTCTGCGGTGGACAGCTACTACTACGATGATG GTCAGGTTCTCCCCGGTTCACAGAGGTCAGGGÅGTTTGCCATTGTT CCCCTGCATGCGGCCCCGGGGGACGCAGTAGCCGAGATCGACGCTCT CTATGACGTCTACCTGGATGTCCAAGAGAAATGGGGCTTGGAGGACG TCATGTTGATGGGCGACTTCAATGCGGGCTGCAGCTATGTGAGACCCT CCCAGTGGTCATCCATCCGCCTGTGGACAAGCCCCACCTTCCAGTGGC TGATCCCGACAGCGCTGACACCACAGCTACACCCACGCACTGTGCCT ATGACAGGATCGTGGTTGCAGGGATGCTGCTCCGAGGCGCCGTTGTTC CCGACTCGGCTCTTCCCTTTAACTTCCAGGCTGCCTATGGCCTGAGTG ACCAACTGGCCCAAGCCATCAGTGACCACTATCCAGTGGAGGTGATG CTGAAGTGAGCAGCCCCTCCCCACACCAGTTGAACTGCAG

FIG. 74B

Met Arg Gly Met Lys Leu Leu Gly Ala Leu Leu Ala Leu Ala Ala Leu Leu Gln Gly Ala Val Ser Leu Lys Ile Ala Ala Phe Asn Ile Gln Thr Phe Gly Glu Thr Lys Met Ser Asn Ala Thr Leu Val Ser Tyr Ile Val Gln Ile Leu Ser Arg Tyr Asp Ile Ala Leu Val Gln Glu Val Arg Asp Ser His Leu Thr Ala Val Gly Lys Leu Leu Asp Asn Leu Asn Gln Asp Ala Pro Asp Thr Tyr His Tyr Val Val Ser Glu Pro Leu Gly Arg Asn Ser Tyr Lys Glu Arg Tyr Leu Phe Val Tyr Arg Pro Asp Gln Val Ser Ala Val Asp Ser Tyr Tyr Tyr Asp Asp Gly Cys Glu Pro Cys Gly Asn Asp Thr Phe Asn Arg Glu Pro Ala Ile Val Arg Phe Phe Ser Arg Phe Thr Glu Val Arg Glu Phe Ala Ile Val Pro Leu His Ala Ala Pro Gly Asp Ala Val Ala Glu Ile Asp Ala Leu Tyr Asp Val Tyr Leu Asp Val Gln Glu Lys Trp Gly Leu Glu Asp Val Met Leu Met Gly Asp Phe Asn Ala Gly Cys Ser Tyr Val Arg Pro Ser Gln Trp Ser Ser Ile Arg Leu Trp Thr Ser Pro Thr Phe Gln Trp Leu Ile Pro Asp Ser Ala Asp Thr Thr Ala Thr Pro Thr His Cys Ala Tyr Asp Arg Ile Val Ala Gly Met Leu Leu Arg Gly Ala Val Val Pro Asp Ser Ala Leu Pro Phe Asn Phe Gln Ala Ala Tyr Gly Leu Ser Asp Gln Leu Ala Gln Ala Ile Ser Asp His Tyr Pro Val Glu Val Met Leu Lys

FIG. 75A

FIG. 75B

Met Ala Leu Trp Met Arg Leu Leu Pro Leu Leu Ala Leu Leu Ala Leu Trp Gly Pro Asp Pro Ala Ala Ala Phe Val Asn Gln His Leu Cys Gly Ser His Leu Val Glu Ala Leu Tyr Leu Val Cys Gly Glu Arg Gly Phe Phe Tyr Thr Pro Lys Thr Arg Arg Glu Ala Glu Asp Leu Gln Val Gly Gln Val Glu Leu Gly Gly Gly Pro Gly Ala Gly Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Lys Arg Gly Ile Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn

FIG. 76A

ATGGGAGGTTGGTCTTCCAAACCTCGACAAGGCATGGGGACGAATCT TTCTGTTCCCAATCCTCTGGGATTCTTTCCCGATCACCAGTTGGACCCT GCGTTCGGAGCCAACTCAAACAATCCAGATTGGGACTTCAACCCCAA CAAGGATCACTGGCCAGAGGCAATCAAGGTAGGAGCGGGAGACTTC GGGCCAGGGTTCACCCCACCACACGGCGGTCTTTTGGGGTGGAGCCC TCAGGCTCAGGGCATATTGACAACAGTGCCAGCAGCGCCTCCTCCTG TTTCCACCAATCGGCAGTCAGGAAGACAGCCTACTCCCATCTCTCCAC CTCTAAGAGACAGTCATCCTCAGGCCATGCAGTGGAACTCCACAACA TTCCACCAAGCTCTGCTAGATCCCAGAGTGAGGGGCCTATATTTTCCT GCTGGTGGCTCCAGTTCCGGAACAGTAAACCCTGTTCCGACTACTGTC TCACCCATATCGTCAATCTTCTCGAGGACTGGGGACCCTGCACCGAAC ATGGAGAGCACAACATCAGGATTCCTAGGACCCCTGCTCGTGTTACA GGCGGGGTTTTTCTTGTTGACAAGAATCCTCACAATACCACAGAGTCT AGACTCGTGGTGGACTTCTCTCAATTTTCTAGGGGGAGCACCCACGTG TTGTCCTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTT ATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTGTTGGTTC TTCTGGACTACCAAGGTATGTTGCCCGTTTGTCCTCTACTTCCAGGAA CATCAACTACCAGCACGGGACCATGCAAGACCTGCACGATTCCTGCT CAAGGAACCTCTATGTTTCCCTCTTGTTGCTGTACAAAACCTTCGGAC GGAAACTGCACTTGTATTCCCATCCCATCATCCTGGGCTTTCGCAAGA TTCCTATGGGAGTGGGCCTCAGTCCGTTTCTCCTGGCTCAGTTTACTA GTGCCATTTGTTCAGTGGTTCGCAGGGCTTTCCCCCACTGTTTGGCTTT CAGTTATATGGATGATGTGGTATTGGGGGCCAAGTCTGTACAACATCT TGAGTCCCTTTTTACCTCTATTACCAATTTTCTTTTGTCTTTGGGTATAC ATTTGA

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FIG. 76B

Met Gly Gly Trp Ser Ser Lys Pro Arg Gln Gly Met Gly Thr Asn Leu Ser Val Pro Asn Pro Leu Gly Phe Phe Pro Asp His Gln Leu Asp Pro Ala Phe Gly Ala Asn Ser Asn Asn Pro Asp Trp Asp Phe Asn Pro Asn Lys Asp His Trp Pro Glu Ala Ile Lys Val Gly Ala Gly Asp Phe Gly Pro Gly Phe Thr Pro Pro His Gly Gly Leu Leu Gly Trp Ser Pro Gln Ala Gln Gly Ile Leu Thr Thr Val Pro Ala Ala Pro Pro Pro Val Ser Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro Pro Leu Arg Asp Ser His Pro Gln Ala Met Gln Trp Asn Ser Thr Thr Phe His Gln Ala Leu Leu Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro Ala Gly Gly Ser Ser Ser Gly Thr Val Asn Pro Val Pro Thr Thr Val Ser Pro Ile Ser Ser Ile Phe Ser Arg Thr Gly Asp Pro Ala Pro Asn Met Glu Ser Thr Thr Ser Gly Phe Leu Gly Pro Leu Leu Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Ala Pro Thr Cys Pro Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro Pro Ile Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu Leu Pro Gly Thr Ser Thr Thr Ser Thr Gly Pro Cys Lys Thr Cys Thr Ile Pro Ala Gln Gly Thr Ser Met Phe Pro Ser Cys Cys Cys Thr Lys Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Ala Arg Phe Leu Trp Glu Trp Ala Ser Val Arg Phe Ser Trp Leu Ser Leu Leu Val Pro Phe Val Gln Trp Phe Ala Gly Leu Ser Pro Thr Val Trp Leu Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro Ser Leu Tyr Asn Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys Leu Trp Val Tyr Ile

FIG. 77A

CGAACCACTCAGGGTCCTGTGGACAGCTCACCTAGCTGCAATGGCTA CCTGGCTTCAAGAGGGCAGTGCCTTCCCAACCATTCCCTTATCCAGGC CTTTTGACAACGCTATGCTCCGCGCCCATCGTCTGCACCAGCTGGCCT TTGACACCTACCAGGAGTTTGAAGAAGCCTATATCCCAAAGGAACAG AAGTATTCATTCCTGCAGAACCCCCAGACCTCCCTCTGTTTCTCAGAG TCTATTCCGACACCCTCCAACAGGGAGGAAACACAACAGAAATCCAA CCTAGAGCTGCTCCGCATCTCCCTGCTGCTCATCCAGTCGTGGCTGGA GCCCGTGCAGTTCCTCAGGAGTGTCTTCGCCAACAGCCTGGTGTACGG CGCCTCTGACAGCAACGTCTATGACCTCCTAAAGGACCTAGAGGAAG GCATCCAAACGCTGATGGGGAGGCTGGAAGATGGCAGCCCCCGGACT GGGCAGATCTTCAAGCAGACCTACAGCAAGTTCGACACAAACTCACA CAACGATGACGCACTACTCAAGAACTACGGGCTGCTCTACTGCTTCAG GAAGGACATGCCAAGGTCGAGACATTCCTGCGCATCGTGCAGTGCCG CTCTGTGGAGGGCAGCTGTGGCTTCTAGCTGCCCGGGTGGCATCCCTG TGACCCCTCCCCAGTGCCTCTCCTGGCCCTGGAAGTTGCCACTCCAGT GCCCACCAGCCTTGTCCTAATAAAATTAAGTTGCATC

FIG. 77B

Met Ala Thr Gly Ser Arg Thr Ser Leu Leu Leu Ala Phe Gly Leu Leu Cys Leu Pro Trp Leu Gln Glu Gly Ser Ala Phe Pro Thr Ile Pro Leu Ser Arg Pro Phe Asp Asn Ala Met Leu Arg Ala His Arg Leu His Gln Leu Ala Phe Asp Thr Tyr Gln Glu Phe Glu Glu Ala Tyr Ile Pro Lys Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro Gln Thr Ser Leu Cys Phe Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg Glu Glu Thr Gln Gln Lys Ser Asn Leu Glu Leu Leu Arg Ile Ser Leu Leu Leu Ile Gln Ser Trp Leu Glu Pro Val Gln Phe Leu Arg Ser Val Phe Ala Asn Ser Leu Val Tyr Gly Ala Ser Asp Ser Asn Val Tyr Asp Leu Leu Lys Asp Leu Glu Glu Gly Ile Gln Thr Leu Met Gly Arg Leu Glu Asp Gly Ser Pro Arg Thr Gly Gln Ile Phe Lys Gln Thr Tyr Ser Lys Phe Asp Thr Asn Ser His Asn Asp Asp Ala Leu Leu Lys Asn Tyr Gly Leu Leu Tyr Cys Phe Arg Lys Asp Met Asp Lys Val Glu Thr Phe Leu Arg Ile Val Gln CysArg Ser Val Glu Gly Ser Cys Gly Phe

FIG. 78A

TTATCTTTTGTCCTTGCTGCTCATTGGCTTCTGGGACTGCGTGACCTGT CACGGGAGCCCTGTGGACATCTGCACAGCCAAGCCGCGGGACATTCC CATGAATCCCATGTGCATTTACCGCTCCCCGGAGAAGAAGGCAACTG AGGATGAGGCTCAGAACAGAAGATCCCGGAGGCCACCAACCGGCG TGTCTGGGAACTGTCCAAGGCCAATTCCCGCTTTGCTACCACTTTCTA TCAGCACCTGGCAGATTCCAAGAATGACAATGATAACATTTTCCTGTC ACCCCTGAGTATCTCCACGGCTTTTGCTATGACCAAGCTGGGTGCCTG TAATGACACCCTCCAGCAACTGATGGAGGTATTTAAGTTTGACACCAT ATCTGAGAAAACATCTGATCAGATCCACTTCTTTGCCAAACTGAA CTGCCGACTCTATCGAAAAGCCAACAAATCCTCCAAGTTAGTATCAGC CAATCGCCTTTTTGGAGACAAATCCCTTACCTTCAATGAGACCTACCA GGACATCAGTGAGTTGGTATATGGAGCCAAGCTCCAGCCCCTGGACT TCAAGGAAAATGCAGAGCAATCCAGAGCGCCATCAACAAATGGGTG TCCAATAAGACCGAAGCCGAATCACCGATGTCATTCCCTCGGAAGC CATCAATGAGCTCACTGTTCTGGTGCTGGTTAACACCCATTTACTTCAA TGTTCTACAAGGCTGATGGAGAGTCGTGTTCAGCATCTATGATGTACC AGGAAGGCAAGTTCCGTTATCGGCGCGTGGCTGAAGGCACCCAGGTG CTTGAGTTGCCCTTCAAAGGTGATGACATCACCATGGTCCTCATCTTG CCCAAGCCTGAGAAGAGCCTGGCCAAGGTGGAGAAGGAACTCACCCC AGAGGTGCTGCAGGAGTGGCTGGATGAATTGGAGGAGATGATGCTGG TGGTCCACATGCCCCGCTTCCGCATTGAGGACGGCTTCAGTTTGAAGG AGCAGCTGCAAGACATGGGCCTTGTCGATCTGTTCAGCCCTGAAAAG TCCAAACTCCCAGGTATTGTTGCAGAAGGCCGAGATGACCTCTATGTC TCAGATGCATTCCATAAGGCATTTCTTGAGGTAAATGAAGAAGGCAG TGAAGCAGCTGCAAGTACCGCTGTTGTGATTGCTGGCCGTTCGCTAAA CCCCAACAGGGTGACTTTCAAGGCCAACAGGCCTTTCCTGGTTTTTAT AAGAGAAGTTCCTCTGAACACTATTATCTTCATGGGCAGAGTAGCCA ACCCTTGTGTTAAGTAA

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FIG. 78B

Met Tyr Ser Asn Val Ile Gly Thr Val Thr Ser Gly Lys Arg Lys Val Tyr Leu Leu Ser Leu Leu Leu Ile Gly Phe Trp Asp Cys Val Thr Cys His Gly Ser Pro Val Asp Ile Cys Thr Ala Lys Pro Arg Asp Ile Pro Met Asn Pro Met Cys Ile Tyr Arg Ser Pro Glu Lys Lys Ala Thr Glu Asp Glu Gly Ser Glu Gln Lys Ile Pro Glu Ala Thr Asn Arg Arg Val Trp Glu Leu Ser Lys Ala Asn Ser Arg Phe Ala Thr Thr Phe Tyr Gln His Leu Ala Asp Ser Lys Asn Asp Asn Asp Asn Ile Phe Leu Ser Pro Leu Ser Ile Ser Thr Ala Phe Ala Met Thr Lys Leu Gly Ala Cys Asn Asp Thr Leu Gln Gln Leu Met Glu Val Phe Lys Phe Asp Thr Ile Ser Glu Lys Thr Ser Asp Gln Ile His Phe Phe Phe Ala Lys Leu Asn Cys Arg Leu Tyr Arg Lys Ala Asn Lys Ser Ser Lys Leu Val Ser Ala Asn Arg Leu Phe Gly Asp Lys Ser Leu Thr Phe Asn Glu Thr Tyr Gln Asp Ile Ser Glu Leu Val Tyr Gly Ala Lys Leu Gln Pro Leu Asp Phe Lys Glu Asn Ala Glu Gln Ser Arg Ala Ala Ile Asn Lys Trp Val Ser Asn Lys Thr Glu Gly Arg Ile Thr Asp Val Ile Pro Ser Glu Ala Ile Asn Glu Leu Thr Val Leu Val Leu Val Asn Thr Ile Tyr Phe Lys Gly Leu Trp Lys Ser Lys Phe Ser Pro Glu Asn Thr Arg Lys Glu Leu Phe Tyr Lys Ala Asp Gly Glu Ser Cys Ser Ala Ser Met Met Tyr Gin Glu Gly Lys Phe Arg Tyr Arg Arg Val Ala Glu Gly Thr Gln Val Leu Glu Leu Pro Phe Lys Gly Asp Asp Ile Thr Met Val Leu Ile Leu Pro Lys Pro Glu Lys Ser Leu Ala Lys Val Glu Lys Glu Leu Thr Pro Glu Val Leu Gln Glu Trp Leu Asp Glu Leu Glu Glu Met Met Leu Val Val His Met Pro Arg Phe Arg Ile Glu Asp Gly Phe Ser Leu Lys Glu Gln Leu Gln Asp Met Gly Leu Val Asp Leu Phe Ser Pro Glu Lys Ser Lys Leu Pro Gly Ile Val Ala Glu Gly Arg Asp Asp Leu Tyr Val Ser Asp Ala Phe His Lys Ala Phe Leu Glu Val Asn Glu Glu Gly Ser Glu Ala Ala Ala Ser Thr Ala Val Val Ile Ala Gly Arg Ser Leu Asn Pro Asn Arg Val Thr Phe Lys Ala Asn Arg Pro Phe Leu Val Phe Ile Arg Glu Val Pro Leu Asn Thr Ile Ile Phe Met Gly Arg Val Ala Asn Pro Cys Val Lys

FIG. 79A

ATGGATTACTACAGAAAATATGCAGCTATCTTCTGGTCACATTGTCG
GTGTTTCTGCATGTTCTCCATTCCGCTCCTGATGTGCAGGATTGCCCAG
AATGCACGCTACAGGAAAACCCATTCTTCTCCCAGCCGGGTGCCCCA
ATACTTCAGTGCATGGGCTGCTGCTTCTCTAGAGCATATCCCACTCCA
CTAAGGTCCAAGAAGACGATGTTGGTCCAAAAGAACGTCACCTCAGA
GTCCACTTGCTGTGTAGCTAAATCATATAACAGGGTCACAGTAATGGG
GGGTTTCAAAGTGGAGAACCACACGGCGTGCCACTGCAGTACTTGTT
ATTATCACAAATCTTAA

FIG. 79B

Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser Val Phe Leu His Val Leu His Ser Ala Pro Asp Val Gln Asp Cys Pro Glu Cys Thr Leu Gln Glu Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro Ile Leu Gln Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn Val Thr Ser Glu Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr Tyr His Lys Ser

FIG. 79C

FIG. 79D

Met Glu Met Phe Gln Gly Leu Leu Leu Leu Leu Leu Leu Ser Met Gly Gly Thr Trp Ala Ser Lys Glu Pro Leu Arg Pro Arg Cys Arg Pro Ile Asn Ala Thr Leu Ala Val Glu Lys Glu Gly Cys Pro Val Cys Ile Thr Val Asn Thr Thr Ile Cys Ala Gly Tyr Cys Pro Thr Met Thr Arg Val Leu Gln Gly Val Leu Pro Ala Leu Pro Gln Val Val Cys Asn Tyr Arg Asp Val Arg Phe Glu Ser Ile Arg Leu Pro Gly Cys Pro Arg Gly Val Asn Pro Val Val Ser Tyr Ala Val Ala Leu Ser Cys Gln Cys Ala Leu Cys Arg Arg Ser Thr Thr Asp Cys Gly Gly Pro Lys Asp His Pro Leu Thr Cys Asp Asp Pro Arg Phe Gln Asp Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro Gln

FIG. 80A

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ATGCGTCCCTGCGCCCCCGCGCGCGCTGCTGGCCTCCTGGCCTCG CTCCTGGCCGCCCCCGGTGGCCCCGGCCGAGGCCCCGCACCTGGT GCAGGTGGACGCGCCCCGCGCGCTGTGGCCCCTGCGGCGCTTCTGGA GGAGCACAGGCTTCTGCCCCCCGCTGCCACACAGCCAGGCTGACCAG TACGTCCTCAGCTGGGACCAGCAGCTCAACCTCGCCTATGTGGGCGCC GTCCCTCACCGCGCATCAAGCAGGTCCGGACCCACTGGCTGCTGGA GCTTGTCACCACCAGGGGGTCCACTGGACGGGCCTGAGCTACAACT TCACCCACCTGGACGGGTACTTGGACCTTCTCAGGGAGAACCAGCTCC TCCCAGGGTTTGAGCTGATGGGCAGCGCCTCGGGCCACTTCACTGACT TTGAGGACAAGCAGCAGGTGTTTGAGTGGAAGGACTTGGTCTCCAGC CTGGCCAGGAGATACATCGGTAGGTACGGACTGGCGCATGTTTCCAA GTGGAACTTCGAGACGTGGAATGAGCCAGACCACCACGACTTTGACA ACGTCTCCATGACCATGCAAGGCTTCCTGAACTACTACGATGCCTGCT GGCGACTCCTTCCACACCCCACCGCGATCCCCGCTGAGCTGGGGCCTC CTGCGCCACTGCCACGACGGTACCAACTTCTTCACTGGGGAGGCGGG CGTGCGGCTGGACTACATCTCCCTCCACAGGAAGGGTGCGCGCAGCT CCATCTCCATCCTGGAGCAGGAGAAGGTCGTCGCGCAGCAGATCCGG CAGCTCTTCCCCAAGTTCGCGGACACCCCCATTTACAACGACGAGGCG GACCCGCTGGTGGCTGGTCCCTGCCACAGCCGTGGAGGGCGGACGT GACCTACGCGCCATGGTGGTGAAGGTCATCGCGCAGCATCAGAACC TGCTACTGGCCAACACCACCTCCGCCTTCCCCTACGCGCTCCTGAGCA ACGACAATGCCTTCCTGAGCTACCACCCGCACCCCTTCGCGCAGCGCA CAGCTGTTGCGCAAGCCGGTGCTCACGGCCATGGGGCTGCTGGCGCT GCTGGATGAGGAGCAGCTCTGGGCCGAAGTGTCGCAGGCCGGGACCG TCCTGGACAGCAACCACACGGTGGGCGTCCTGGCCAGCGCCCACCGC CCCCAGGCCCGCCGACGCCTGCCGCGCGCGCGTGCTGATCTACGC GAGCGACGACCCCGCGCCCCACCCCAACCGCAGCGTCGCGGTGACCC TGCGGCTGCGCGGGTGCCCCCCGGCCCGGCCTGGTCTACGTCACG CGCTACCTGGACAACGGGCTCTGCAGCCCCGACGGCGAGTGGCGGCG CCTGGGCCGGCCGTCTTCCCCACGGCAGAGCAGTTCCGGCGCATGC GCGCGGCTGAGGACCCGGTGGCCGCGCGCCCCCTTACCCGCC GGCGGCCGCCTGACCCTGCGCCCCGCGCTGCGGCTGCCGTCGCTTTTG CTGGTGCACGTGTGTGCGCGCCCCGAGAAGCCGCCCGGGCAGGTCAC GCGGCTCCGCCCCTGCCCCTGACCCAAGGGCAGCTGGTTCTGGTCTG GTCGGATGAACACGTGGGCTCCAAGTGCCTGTGGACATACGAGATCC AGTTCTCTCAGGACGGTAAGGCGTACACCCCGGTCAGCAGGAAGCCA TCGACCTTCAACCTCTTTGTGTTCAGCCCAGACACAGGTGCTGTCTCT GGCTCCTACCGAGTTCGAGCCCTGGACTACTGGGCCCGACCAGGCCC CTTCTCGGACCCTGTGCCGTACCTGGAGGTCCCTGTGCCAAGAGGGCC CCCATCCCCGGGCAATCCAT GA

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FIG. 80B

Met Arg Pro Leu Arg Pro Arg Ala Ala Leu Leu Ala Leu Leu Ala Ser Leu Leu Ala Ala Pro Pro Val Ala Pro Ala Glu Ala Pro His Leu Val Gln Val Asp Ala Ala Arg Ala Leu Trp Pro Leu Arg Arg Phe Trp Arg Ser Thr Gly Phe Cys Pro Pro Leu Pro His Ser Gln Ala Asp Gln Tyr Val Leu Ser Trp Asp Gln Gln Leu Asn Leu Ala Tyr Val Gly Ala Val Pro His Arg Gly Ile Lys Gln Val Arg Thr His Trp Leu Leu Glu Leu Val Thr Thr Arg Gly Ser Thr Gly Arg Gly Leu Ser Tyr Asn Phe Thr His Leu Asp Gly Tyr Leu Asp Leu Leu Arg Glu Asn Gln Leu Leu Pro Gly Phe Glu Leu Met Gly Ser Ala Ser Gly His Phe Thr Asp Phe Glu Asp Lys Gln Gln Val Phe Glu Trp Lys Asp Leu Val Ser Ser Leu Ala Arg Arg Tyr Ile Gly Arg Tyr Gly Leu Ala His Val Ser Lys Trp Asn Phe Glu Thr Trp Asn Glu Pro Asp His His Asp Phe Asp Asn Val Ser Met Thr Met Gln Gly Phe Leu Asn Tyr Tyr Asp Ala Cys Ser Glu Gly Leu Arg Ala Ala Ser Pro Ala Leu Arg Leu Gly Gly Pro Gly Asp Ser Phe His Thr Pro Pro Arg Ser Pro Leu Ser Trp Gly Leu Leu Arg His Cys His Asp Gly Thr Asn Phe Phe Thr Gly Glu Ala Gly Val Arg Leu Asp Tyr Ile Ser Leu His Arg Lys Gly Ala Arg Ser Ser Ile Ser Ile Leu Glu Gln Glu Lys Val Val Ala Gln Gln Ile Arg Gln Leu Phe Pro Lys Phe Ala Asp Thr Pro Ile Tyr Asn Asp Glu Ala Asp Pro Leu Val Gly Trp Ser Leu Pro Gln Pro Trp Arg Ala Asp Val Thr Tyr Ala Ala Met Val Val Lys Val Ile Ala Gln His Gln Asn Leu Leu Leu Ala Asn Thr Thr Ser Ala Phe Pro Tyr Ala Leu Leu Ser Asn Asp Asn Ala Phe Leu Ser Tyr His Pro His Pro Phe Ala Gln Arg Thr Leu Thr Ala Arg Phe Gln Val Asn Asn Thr Arg Pro Pro His Val Gln Leu Leu Arg Lys Pro Val Leu Thr Ala Met Gly Leu Leu Ala Leu Leu Asp Glu Glu Gln Leu Trp Ala Glu Val Ser Gln Ala Gly Thr Val Leu Asp Ser Asn His Thr Val Gly Val Leu Ala Ser Ala His Arg Pro Gln Gly Pro Ala Asp Ala Trp Arg Ala Ala Val Leu Ile Tyr Ala Ser Asp Asp Thr Arg Ala His Pro Asn Arg Ser Val Ala Val Thr Leu Arg Leu Arg Gly Val Pro Pro Gly Pro Gly Leu Val Tyr Val Thr Arg Tyr Leu Asp Asn Gly Leu Cys Ser Pro Asp Gly Glu Trp Arg Arg Leu Gly Arg Pro Val Phe Pro Thr Ala Glu Gln Phe Arg Arg Met Arg Ala Ala Glu Asp Pro Val Ala Ala Ala Pro Arg Pro Leu Pro Ala Gly Gly Arg Leu Thr Leu Arg Pro Ala Leu Arg Leu Pro Ser Leu Leu Leu Val His Val Cys Ala Arg Pro Glu Lys Pro Pro Gly Gln Val Thr Arg Leu Arg Ala Leu Pro Leu Thr Gln Gly Gln Leu Val Leu Val Trp Ser Asp Glu His Val Gly Ser Lys Cys Leu Trp Thr Tyr Glu Ile Gln Phe Ser Gln Asp Gly Lys Ala Tyr Thr Pro Val Ser Arg Lys Pro Ser Thr Phe Asn Leu Phe Val Phe Ser Pro Asp Thr Gly Ala Val Ser Gly Ser Tyr Arg Val Arg Ala Leu Asp Tyr Trp Ala Arg Pro Gly Pro Phe Ser Asp Pro Val Pro Tyr Leu Glu Val Pro Val Pro Arg Gly Pro Pro Ser Pro Gly Asn Pro

FIG. 81A

ATGCAGCTGAGGAACCCAGAACTACATCTGGGCTGCGCGCTTGCGCT TCGCTTCCTGGCCCTCGTTTCCTGGGACATCCCTGGGGCTAGAGCACT AGCGCTTCATGTGCAACCTTGACTGCCAGGAAGAGCCAGATTCCTGC ATCAGTGAGAAGCTCTTCATGGAGATGGCAGAGCTCATGGTCTCAGA AGGCTGGAAGGATGCAGGTTATGAGTACCTCTGCATTGATGACTGTTG GATGGCTCCCCAAAGAGATTCAGAAGGCAGACTTCAGGCAGACCCTC AGCGCTTTCCTCATGGGATTCGCCAGCTAGCTAATTATGTTCACAGCA AAGGACTGAAGCTAGGGATTTATGCAGATGTTGGAAATAAAACCTGC GCAGGCTTCCCTGGGAGTTTTGGATACTACGACATTGATGCCCAGACC TTTGCTGACTGGGGAGTAGATCTGCTAAAATTTGATGGTTGTTACTGT GACAGTTTGGAAAATTTGGCAGATGGTTATAAGCACATGTCCTTGGCC CTGAATAGGACTGGCAGAAGCATTGTGTACTCCTGTGAGTGGCCTCTT TATATGTGGCCCTTTCAAAAGCCCAATTATACAGAAATCCGACAGTAC TGCAATCACTGGCGAAATTTTGCTGACATTGATGATTCCTGGAAAAGT ATAAAGAGTATCTTGGACTGGACATCTTTTAACCAGGAGAGAATTGTT GATGTTGCTGGACCAGGGGGTTGGAATGACCCAGATATGTTAGTGAT TGGCAACTTTGGCCTCAGCTGGAATCAGCAAGTAACTCAGATGGCCCT CTGGGCTATCATGGCTCCTTTATTCATGTCTAATGACCTCCGACA CATCAGCCCTCAAGCCAAAGCTCTCCTTCAGGATAAGGACGTAATTGC CATCAATCAGGACCCCTTGGGCAAGCAAGGGTACCAGCTTAGACAGG GAGACAACTTTGAAGTGTGGGAACGACCTCTCTCAGGCTTAGCCTGG GCTGTAGCTATGATAAACCGGCAGGAGATTGGTGGACCTCGCTCTTAT ACCATCGCAGTTGCTTCCCTGGGTAAAGGAGTGGCCTGTAATCCTGCC TGCTTCATCACACAGCTCCTCCCTGTGAAAAGGAAGCTAGGGTTCTAT GAATGGACTTCAAGGTTAAGAAGTCACATAAATCCCACAGGCACTGT TTTGCTTCAGCTAGAAAATACAATGCAGATGTCATTAAAAGACTTACT TTAA

FIG. 81B

Met Gln Leu Arg Asn Pro Glu Leu His Leu Gly Cys Ala Leu Ala Leu Arg Phe Leu Ala Leu Val Ser Trp Asp Ile Pro Gly Ala Arg Ala Leu Asp Asn Gly Leu Ala Arg Thr Pro Thr Met Gly Trp Leu His Trp Glu Arg Phe Met Cys Asn Leu Asp Cys Gln Glu Glu Pro Asp Ser Cys Ile Ser Glu Lys Leu Phe Met Glu Met Ala Glu Leu Met Val Ser Glu Gly Trp Lys Asp Ala Gly Tyr Glu Tyr Leu Cys Ile Asp Asp Cys Trp Met Ala Pro Gln Arg Asp Ser Glu Gly Arg Leu Gln Ala Asp Pro Gln Arg Phe Pro His Gly Ile Arg Gln Leu Ala Asn Tyr Val His Ser Lys Gly Leu Lys Leu Gly Ile Tyr Ala Asp Val Gly Asn Lys Thr Cys Ala Gly Phe Pro Gly Ser Phe Gly Tyr Tyr Asp Ile Asp Ala Gln Thr Phe Ala Asp Trp Gly Val Asp Leu Leu Lys Phe Asp Gly Cys Tyr Cys Asp Ser Leu Glu Asn Leu Ala Asp Gly Tyr Lys His Met Ser Leu Ala Leu Asn Arg Thr Gly Arg Ser Ile Val Tyr Ser Cys Glu Trp Pro Leu Tyr Met Trp Pro Phe Gln Lys Pro Asn Tyr Thr Glu Ile Arg Gln Tyr Cys Asn His Trp Arg Asn Phe Ala Asp Ile Asp Asp Ser Trp Lys Ser Ile Lys Ser Ile Leu Asp Trp Thr Ser Phe Asn Gln Glu Arg Ile Val Asp Val Ala Gly Pro Gly Gly Trp Asn Asp Pro Asp Met Leu Val Ile Gly Asn Phe Gly Leu Ser Trp Asn Gln Gln Val Thr Gln Met Ala Leu Trp Ala Ile Met Ala Ala Pro Leu Phe Met Ser Asn Asp Leu Arg His Ile Ser Pro Gln Ala Lys Ala Leu Leu Gln Asp Lys Asp Val Ile Ala Ile Asn Gln Asp Pro Leu Gly Lys Gln Gly Tyr Gln Leu Arg Gln Gly Asp Asn Phe Glu Val Trp Glu Arg Pro Leu Ser Gly Leu Ala Trp Ala Val Ala Met Ile Asn Arg Gln Glu Ile Gly Gly Pro Arg Ser Tyr Thr Ile Ala Val Ala Ser Leu Gly Lys Gly Val Ala Cys Asn Pro Ala Cys Phe Ile Thr Gln Leu Leu Pro Val Lys Arg Lys Leu Gly Phe Tyr Glu Trp Thr Ser Arg Leu Arg Ser His Ile Asn Pro Thr Gly Thr Val Leu Leu Gln Leu Glu Asn Thr Met Gln Met Ser Leu Lys Asp Leu Leu

FIG. 82A

ATGGCGCCCGTCGCCGTCTGGGCCGCCGTCGGACTGGAGCT CTGGGCTGCGGCACGCCTTGCCCGCCCAGGTGGCATTTACACCCTA · CGCCCGGAGCCCGGGAGCACATGCCGGCTCAGAGAATACTATGACC AGACAGCTCAGATGTGCTGCAGCAAATGCTCGCCGGGCCAACATGCA AAAGTCTTCTGTACCAAGACCTCGGACACCGTGTGTGACTCCTGTGAG GACAGCACATACACCCAGCTCTGGAACTGGGTTCCCGAGTGCTTGAG CTGTGGCTCCCGCTGTAGCTCTGACCAGGTGGAAACTCAAGCCTGCAC TCGGGAACAGAACCGCATCTGCACCTGCAGGCCCGGCTGGTACTGCG CGCTGAGCAAGCAGGAGGGGTGCCGGCTGTGCGCGCCGCTGCGCAAG TGCCGCCCGGGCTTCGGCGTGGCCAGACCAGGAACTGAAACATCAGA CGTGGTGTGCAAGCCCTGTGCCCCGGGGACGTTCTCCAACACGACTTC ATCCACGGATATTTGCAGGCCCCACCAGATCTGTAACGTGGTGGCCAT CCCTGGGAATGCAAGCATGGATGCAGTCTGCACGTCCACGTCCCCCA ACACGATCCCAACACACGCAGCCAACTCCAGAACCCAGCACTGCTCC AAGCACCTCCTTCCTGCTCCCAATGGGCCCCAGCCCCCAGCTGAAGG GAGCACTGGCGACTTCGCTCTTCCAGTTGGACTGATTGTGGGTGTGAC AGCCTTGGGTCTACTAATAATAGGAGTGGTGAACTGTGTCATCATGAC CCAGGTGAAAAAGAAGCCCTTGTGCCTGCAGAGAGAAGCCAAGGTGC CTCACTTGCCTGCCGATAAGGCCCGGGGTACACAGGGCCCCGAGCAG CAGCACCTGCTGATCACAGCGCCGAGCTCCAGCAGCAGCTCCCTGGA GAGCTCGGCCAGTGCGTTGGACAGAAGGGCGCCCACTCGGAACCAGC CACAGGCACCAGGCGTGGAGGCCAGTGGGGCCCGGGGCCCGGGC CAGCACCGGGAGCTCAGATTCTTCCCCTGGTGGCCATGGGACCCAGG TCAATGTCACCTGCATCGTGAACGTCTGTAGCAGCTCTGACCACAGCT CACAGTGCTCCCCAAGCCAGCTCCACAATGGGAGACACAGATTCC AGCCCTCGGAGTCCCCGAAGGACGAGCAGGTCCCCTTCTCCAAGGA GGAATGTGCCTTTCGGTCACAGCTGGAGACGCCAGAGACCCTGCTGG GGAGCACCGAAGAGAGCCCCTGCCCCTTGGAGTGCCTGATGCTGGG ATGAAGCCCAGTTAACCAGGCCGGTGTGGGCTGTGTCGTAGCCAAGG TGGGCTGAGCCCTGGCAGGATGACCCTGCGAAGGGGCCCTGGTCCTT **CCAGGC**

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FIG. 82B

Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly Leu Leu Ile Ile Gly Val Val Asn Cys Val lle Met Thr Gln Val Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser

FIG. 83A

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

FIG. 83B

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

FIG. 84A

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser Gly Met Ser Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Ala Leu Glu Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp Tyr Asn Pro Ser Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Val Leu Lys Val Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Ser Met Ile Thr Asn Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser

FIG. 84B

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Cys Gln Leu Ser Val Gly Tyr Met His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Phe Gln Gly Ser Gly Tyr Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

FIG. 85A

GACATCTTGCTGACTCAGTCTCCAGCCATCCTGTCTGAGTCCAGGA
GAAAGAGTCAGTTTCTCCTGCAGGGCCAGTCAGTTCGTTGGCTCAAGC
ATCCACTGGTATCAGCAAAGAACAAATGGTTCTCCAAGGCTTCTCATA
AAGTATGCTTCTGAGTCTATGTCTGGGATCCCTTCCAGGTTTAGTGGC
AGTGGATCAGGGACAGATTTTACTCTTAGCATCAACACTGTGGAGTCT
GAAGATATTGCAGATTATTACTGTCAACAAAGTCATAGCTGGCCATTC
ACGTTCGGCTCGGGGACAAATTTGGAAGTAAAAGAAGTGAAGCTTGA
GGAGTCTGGAGGAGGCTTGGTGCAACCTGGAGGATCCATGAAACTCT
CCTGTGTTGCCTCTGGATTCATTTTCAGTAACCACTGGATGAACTGGG
TCCGCCAGTCTCCAGAGAAGGGGCTTGAGTGGGTTGCTGAAATTAGA
TCAAAATCTATTAATTCTGCAACACATTATGCGGAGTCTGTGAAAGGG
AGGTTCACCATCTCAAGAGATGATTCCAAAAAGTGCTGTCTACCTGCAA
ATGACCGACTTAAGAACTGAAGACACTGGCGTTTATTACTGTTCCAGG
AATTACTACGGTAGTACCTACGACTACTGGGGCCAAAGGCACCACTCTC
ACAGTCTCC

FIG. 85B

Asp Ile Leu Leu Thr Gln Ser Pro Ala Ile Leu Ser Val Ser Pro Gly Glu Arg Val Ser Phe Ser Cys Arg Ala Ser Gln Phe Val Gly Ser Ser Ile His Trp Tyr Gln Gln Arg Thr Asn Gly Ser Pro Arg Leu Leu Ile Lys Tyr Ala Ser Glu Ser Met Ser Gly Ile Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn Thr Val Glu Ser Glu Asp Ile Ala Asp Tyr Tyr Cys Gln Gln Ser His Ser Trp Pro Phe Thr Phe Gly Ser Gly Thr Asn Leu Glu Val Lys Glu Val Lys Leu Glu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Met Lys Leu Ser Cys Val Ala Ser Gly Phe Ile Phe Ser Asn His Trp Met Asn Trp Val Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val Ala Glu Ile Arg Ser Lys Ser Ile Asn Ser Ala Thr His Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ala Val Tyr Leu Gln Met Thr Asp Leu Arg Thr Glu Asp Thr Gly Val Tyr Tyr Cys Ser Arg Asn Tyr Tyr Gly Ser Thr Tyr Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val Ser

FIG. 86A

ATGGAGACACACTCCTGTTATGGGTGCTGCTGCTCTGGGTTCCA GGTTCCACTGGTGACGTCAGGCGAGGCCCCGGAGCCTGCGGGGCAG GGACGCCCACGCCCTGCGTCCCGGCCGAGTGCTTCGACC TGCTGGTCCGCCACTGCGTGGCCTGCGGGCTCCTGCGCACGCCGCGC CGAAACCGGCCGGGCCAGCAGCCCTGCGCCCAGGACGGCGCTGCAG CCGCAGGAGTCGGTGGCCGGGGGGGCGGCGGCGACA AAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGA CCGTCAGTCTTCCCCCCAAAACCCAAGGACACCCTCATGATC TCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGA AGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGC ATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTA CCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGG CAAGGAGTACAAGTGCAAGGTCTCCAACAAGCCCTCCCAGCCCCCA TCGAGAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCATCCCGGGATGAGCTGACCAAGAACCAGGT CAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGT GGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACG CCTCCCGTGTTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTC ACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTC CGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCTCCCGGGAAATGA

FIG. 86B

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Val Arg Arg Gly Pro Arg Ser Leu Arg Gly Arg Asp Ala Pro Ala Pro Thr Pro Cys Val Pro Ala Glu Cys Phe Asp Leu Leu Val Arg His Cys Val Ala Cys Gly Leu Leu Arg Thr Pro Arg Pro Lys Pro Ala Gly Ala Ser Ser Pro Ala Pro Arg Thr Ala Leu Gln Pro Gln Glu Ser Val Gly Ala Gly Ala Gly Glu Ala Ala Val Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

FIG. 87

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Ile Val Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

FIG. 88

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Gly Pro Gly Thr Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ala

FIG. 89

Asp Ile Gln Met Thr Gln Thr Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys

FIG. 90

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

FIG. 91

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Asp Ile Gln Met Thr Gln Thr Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

FIG. 92

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly

FIG. 93A

FIG. 93B

Met Asp Phe Gln Val Gln Ile Ile Ser Phe Leu Leu Ile Ser Ala Ser Val Ile Met Ser Arg Gly Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile His Trp Phe Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

FIG. 94A

FIG. 94B

Met Gly Trp Ser Leu Ile Leu Leu Phe Leu Val Ala Val Ala Thr Arg Val Leu Ser Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln Thr Pro Gly Arg Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ala

FIG. 95A

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GACGTCGCGGCCCTCTAGGCCTCCAAAAAAGCCTCCTCACTACTTCT AAAATTAGTCAGCCATGCATGGGGGGGAGAATGGGCGGAACTGGGCG GAGTTAGGGGCGGATGGGCGGAGTTAGGGGGCGGGACTATGGTTGCT GACTAATTGAGATGCATGCTTTGCATACTTCTGCCTGCTGGGGAGCCT ATACTTCTGCCTGCGGGGGGCCTGGGGGACTTTCCACACCCTAACTGA CACACATTCCACAGAATTAATTCCCCTAGTTATTAATAGTAATCAATT ACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCC ATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGA CTTTCCATTGACGTCAATGGGTGGACTATTTACGGTAAACTGCCCACT TGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG TCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCT TATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTA TTACCATGGTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGC GGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATG GGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA ACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGG GAGGTCTATATAAGCAGAGCTGGGTACGTGAACCGTCAGATCGCCTG GAGACGCCATCACAGATCTCTCACCATGAGGGTCCCCGCTCAGCTCCT GGGGCTCCTGCTCTGGCTCCCAGGTGCACGATGTGATGGTACCAA GGTGGAAATCAAACGTACGGTGGCTGCACCATCTGTCTTCATCTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCT GCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGG ATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAG GACAGCAAGGACACCTACAGCCTCAGCAGCACCCTGACGCTGAG CAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCC ATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAG TGTTGAATTCAGATCCGTTAACGGTTACCAACTACCTAGACTGGATTC GTGACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTG CCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCCTCCCCGTGCCTTCCT TGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGG AAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTG GGGTGGGCAGGACAGCAAGGGGGGGGGATTGGGAAGACAATAGCAG GCATGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGAC AGCTATGCCAAGTACGCCCCCTATTGACGTCAATGACGGTAAATGGC CCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTT GGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGT TTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGA

FIG. 95B

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CAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTG ACGCAAATGGGCGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAG AGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGAACACAGACCC GTCGACATGGGTTGGAGCCTCATCTTGCTCTTCCTTGTCGCTGTTGCTA CGCGTGTCGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCT CCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTC AAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGC CCTGACCAGCGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGG ACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGG CACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCA AGGTGGACAAGAAAGCAGAGCCCAAATCTTGTGACAAAACTCACACA TGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTC CTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCT GAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGT CAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATGCCAAGA CAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGC GTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGACTACAA GTGCAAGGTCTCCAACAAGCCCTCCCAGCCCCCATCGAGAAAACCA TCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTG CCCCCATCCCGGGATGAGCTGACCAGGAACCAGGTCAGCCTGACCTG CCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTG GACTCCGACGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAG AGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGA GGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGG TAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGTG ACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCCT CCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAA TTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGG TGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCA TGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAGC GCTGGATCTCCCGATCCCCAGCTTTGCTTCTCAATTTCTTATTTGCATA ATGAGAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGAT TGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC AATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGGCAGAGCAT ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGG

FIG. 95C

GCTGCGATTTCGCGCCAAACTTGACGGCAATCCTAGCGTGAAGGCTG GTAGGATTTTATCCCCGCTGCCATCATGGTTCGACCATTGAACTGCAT CGTCGCCGTGTCCCAAAATATGGGGATTGGCAAGAACGGAGACCTAC CCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCCAAAGAATGACC ACAACCTCTTCAGTGGAAGGTAAACAGAATCTGGTGATTATGGGTAG GAAAACCTGGTTCTCCATTCCTGAGAACAATCGACCTTTAAAGGACA GAATTAATATAGTTCTCAGTAGAGAACTCAAAGAACCACCACGAGGA GCTCATTTTCTTGCCAAAAGTTTGGATGATGCCTTAAGACTTATTGAA CAACCGGAATTGGCAAGTAAAGTAGACATGGTTTGGATAGTCGGAGG CAGTTCTGTTTACCAGGAAGCCATGAATCAACCAGGCCACCTTAGACT CTTTGTGACAAGGATCATGCAGGAATTTGAAAGTGACACGTTTTTCCC AGAAATTGATTTGGGGAAATATAAACTTCTCCCAGAATACCCAGGCG TCCTCTCTGAGGTCCAGGAGGAAAAAGGCATCAAGTATAAGTTTGAA GTCTACGAGAAGAAGACTAACAGGAAGATGCTTTCAAGTTCTCTGC TCCCCTCCTAAAGTCATGCATTTTTATAAGACCATGGGACTTTTGCTG TTGCCCCTCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCAC TGTCCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAG AGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCT ATGGAACCAGCTGGGGCTCGAGCTACTAGCTTTGCTTCTCAATTTCTT ATTTGCATAATGAGAAAAAAAGGAAAATTAATTTTAACACCAATTCA GTAGTTGATTGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACA GTGTTCTCTGCACAGATAAGGACAAACATTATTCAGAGGGAGTACCC AGAGCTGAGACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGA AATATGCTTGTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGG TAAGGCCAATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGG CAGAGCATATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTC TGACATAGTTGTGTGGGAGCTTGGATCGATCCTCTATGGTTGAACAA GATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTC GGCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGT GTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGA CCTGTCCGGTGCCCTGAATGAACTGCAGGACGAGGCAGCGCGGCTAT CGTGGCTGGCCACGACGGCGTTCCTTGCGCAGCTGTGCTCGACGTTG TCACTGAAGCGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGG CAGGATCTCCTGTCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATC ATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGC CCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCG GATGGAAGCCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATC AGGGGCTCGCGCCAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATG CCCGACGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCG

FIG. 95D

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AATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGC CGGCTGGGTGTGGCGACCGCTATCAGGACATAGCGTTGGCTACCCG TGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGT GCTTTACGGTATCGCCGCTTCCCGATTCGCAGCGCATCGCCTTCTATC GCCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGAC CGACCAAGCGACGCCAACCTGCCATCACGAGATTTCGATTCCACCG CCGCCTTCTATGAAAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCG GCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCC ACCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATA GCATCACAAATTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTT GTGGTTTGTCCAAACTCATCAATCTATCTATCATGTCTGGATCGCGG CCGCGATCCCGTCGAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCC TGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGG AGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCAC ATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTC GTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTT TGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTC GGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAA TACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGA GCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGC TGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAATC GACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATAC CAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACC CTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTG GCGCTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTC GTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGAC CGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGA CACGACTTATCGCCACTGGCAGCAGCACTGGTAACAGGATTAGCAG AGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTA ACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGA AGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAA CAAACCACCGCTGGTAGCGGTGGTTTTTTTTTTTTTGCAAGCAGCAGATT ACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTAC GGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGG TCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAA AATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTG ACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTC TATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTAC GATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGC GAGACCCACGCTCACCGCCTCCAGATTTATCAGCAATAAACCAGCCA GCCGGAAGGCCCAGCAGCAGCTCCTGCAACTTTATCCGCCTC

FIG. 95E

CAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGG
TGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAAC
GATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAAGCGGTT
AGCTCCTTCGGTCCTCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTG
TTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGC
CATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCAT
TCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAA
TACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATC
ATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTG
TTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCA
GCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGG
CAAAATGCCGCAAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAA
TACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTA
TTGTCTCATGAGCGGATACATATTTGAATGTATTTTAGAAAAAATAAACA
AATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCT

FIG. 96A

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GACGTCGCGGCCGCTCTAGGCCTCCAAAAAAGCCTCCTCACTACTTCT AAAATTAGTCAGCCATGCATGGGGGGGAGAATGGGCGGAACTGGGCG GAGTTAGGGGCGGATTGGTTGCT GACTAATTGAGATGCATGCTTTGCATACTTCTGCCTGCTGGGGAGCCT ATACTTCTGCCTGGGGAGCCTGGGGACTTTCCACACCCTAACTGA CACACATTCCACAGAATTAATTCCCCTAGTTATTAATAGTAATCAATT ACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCC ATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGA CTTTCCATTGACGTCAATGGGTGGACTATTTACGGTAAACTGCCCACT TGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG TCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCT TATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTA TTACCATGGTGATGCGGTTTTTGGCAGTACATCAATGGGCGTGGATACC GGTTTGACTCACGCGGATTTCCAAGTCTCCACCCCATTGACGTCAATG GGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA ACAACTCCGCCCCATTGACGCAAATGGGCGTAGGCGTGTACGGTGG GAGGTCTATATAAGCAGAGCTGGGTACGTGAACCGTCAGATCGCCTG GAGACGCCATCACAGATCTCTCACTATGGATTTTCAGGTGCAGATTAT CAGCTTCCTGCTAATCAGTGCTTCAGTCATAATGTCCAGAGGACAAAT TGTTCTCCCAGTCTCCAGCAATCCTGTCTGCATCTCCAGGGGAGAA GGTCACAATGACTTGCAGGGCCAGCTCAAGTGTAAGTTACATCCACT GGTTCCAGCAGAAGCCAGGATCCTCCCCAAACCCTGGATTTATGCCA CATCCAACCTGGCTTCTGGAGTCCCTGTTCGCTTCAGTGGCAGTGGGT CTGGGACTTCTCACCAATCAGCAGAGTGGAGGCTGAAGATG GAGGGGGACCAAGCTGGAAATCAAACGTACGGTGGCTGCACCATCT GTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCC TCTGTTGTGCCTGAATAACTTCTATCCCAGAGAGGCCAAAGTA CAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAG TGTCACAGAGCAGCAGCAGCACCTACAGCCTCAGCAGCA CCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCC TGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTT CAACAGGGGAGAGTGTTGAATTCAGATCCGTTAACGGTTACCAACTA CCTAGACTGGATTCGTGACAACATGCGGCCGTGATATCTACGTATGAT CAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCTC CCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCC

FIG. 96B

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TAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCT AAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGAACCA GCTGGGGCTCGACAGCTATGCCAAGTACGCCCCCTATTGACGTCAATG ACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGG ACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCAT GGTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTG ACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTT TGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACT CCGCCCATTGACGCAAATGGGCGTAGGCGTGTACGGTGGGAGGTC TATATAAGCAGAGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGA ACACAGACCCGTCGACATGGGTTGGAGCCTCATCTTGCTCTTGT CGCTGTTGCTACGCGTGTCCCAGGTACAACTGCAGCAGCCTGG GGCTGAGCTGAAGCCTGGGGCCTCAGTGAAGATGTCCTGCAAGG CTTCTGGCTACACATTTACCAGTTACAATATGCACTGGGTAAAACAGA CACCTGGTCGGGGCCTGGAATGGATTGGAGCTATTTATCCCGGAAAT GGTGATACTTCCTACAATCAGAAGTTCAAAGGCAAGGCCACATTGAC TGCAGACAAATCCTCCAGCACAGCCTACATGCAGCTCAGCAGCCTGA CATCTGAGGACTCTGCGGTCTATTACTGTGCAAGATCGACTTACTACG GCGGTGACTGCTACTTCAATGTCTGGGGCGCAGGGACCACGGTCACC GTCTCTGCAGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCC TCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGT CAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCG CCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAG GACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGG GCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACC AAGGTGGACAAGAAGCAGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTT CCTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCC TGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGG TCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATGCCAAG ACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAG CGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACA AGTGCAAGGTCTCCAACAAGCCCTCCCAGCCCCCATCGAGAAAACC ATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCT GCCCCATCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAG AGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCT GGACTCCGACGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAA GAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATG AGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGG GTAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGT

FIG. 96C

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GACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCC ACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAA ATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGGTGGG GTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGC ATGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAG CGCTGGATCTCCCGATCCCCAGCTTTGCTTCTCAATTTCTTATTTGCAT AATGAGAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGA TTGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC AATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGGCAGAGCAT ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGGGCTGCGATTTCG CGCCAAACTTGACGCCAATCCTAGCGTGAAGGCTGGTAGGATTTTATC CCCGCTGCCATCATGGTTCGACCATTGAACTGCATCGTCGCCGTGTCC CAAAATATGGGGATTGGCAAGAACGGAGACCTACCCTGGCCTCCGCT CAGGAACGAGTTCAAGTACTTCCAAAGAATGACCACAACCTCTTCAG TGGAAGGTAAACAGAATCTGGTGATTATGGGTAGGAAAACCTGGTTC TCCATTCCTGAGAAGAATCGACCTTTAAAGGACAGAATTAATATAGTT CTCAGTAGAGAACTCAAAGAACCACCACGAGGAGCTCATTTTCTTGC CAAAAGTTTGGATGATGCCTTAAGACTTATTGAACAACCGGAATTGG CAAGTAAAGTAGACATGGTTTGGATAGTCGGAGGCAGTTCTGTTTACC AGGAAGCCATGAATCAACCAGGCCACCTTAGACTCTTTGTGACAAGG ATCATGCAGGAATTTGAAAGTGACACGTTTTTCCCAGAAATTGATTTG GGGAAATATAAACTTCTCCCAGAATACCCAGGCGTCCTCTCTGA GGTCCAGGAGAAAAAGGCATCAAGTATAAGTTTGAAGTCTACGAGA AGAAAGACTAACAGGAAGATGCTTTCAAGTTCTCTGCTCCCCTCCTAA AGCTATGCATTTTTATAAGACCATGGGACTTTTGCTGGCTTTAGATCA GCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCCTCCC CCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTA ATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTAT TCTGGGGGTGGGGTGGGCAGGACAGCAAGGGGGAGGATTGGGAA GACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGAACCAGC TGGGGCTCGAGCTACTAGCTTTGCTTCTCAATTTCTTATTTGCATAATG GCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCTGCA CAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAGACT CCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTTGTC ATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCCAAT CTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGGCAGAGCATATA AGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAGTTG

FIG. 96D

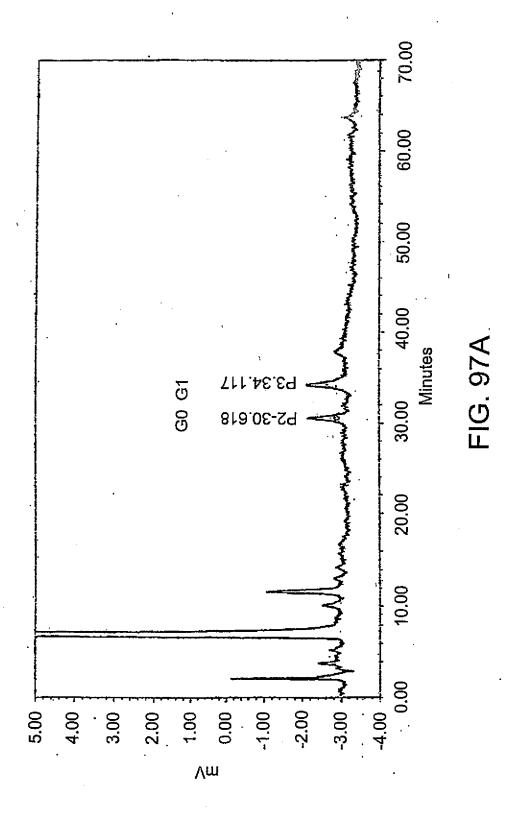
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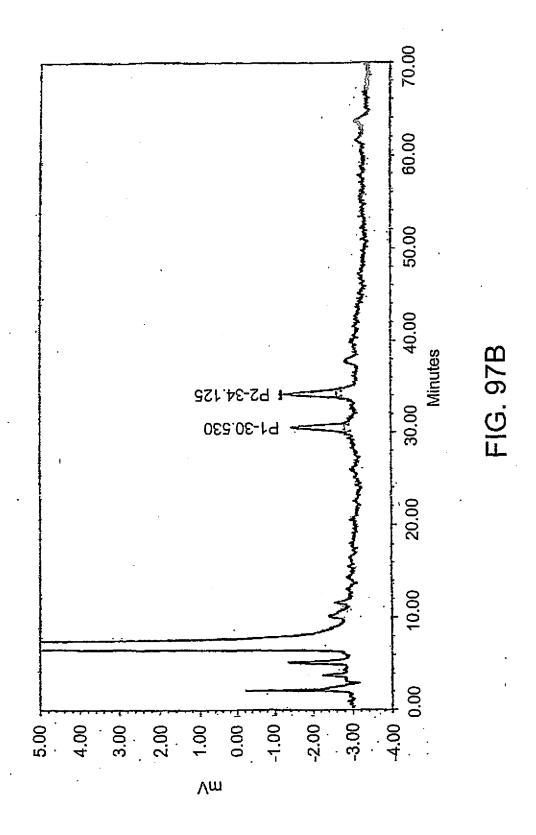
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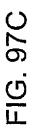
FIG. 96E

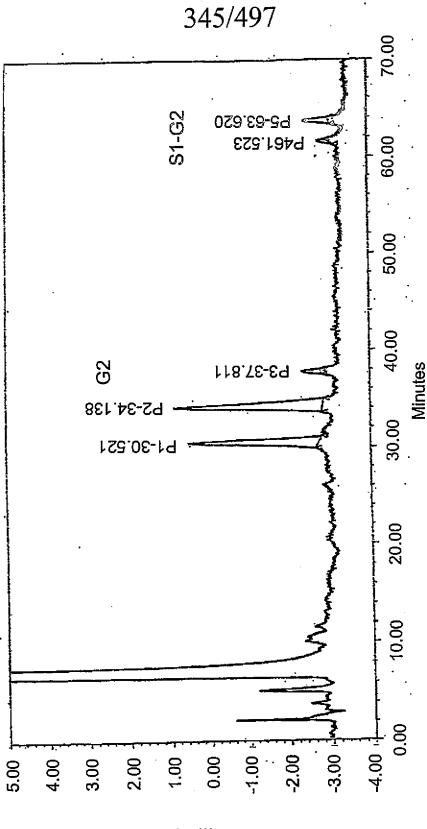
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GCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATG TAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTAC ACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACC TGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAA AAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGC TCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATC AAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAA ATCAATCTAAAGTATATGAGTAAACTTGGTCTGACAGTTACCAATG CTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCC ATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGG CTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTC ACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCG ATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGC GCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGT TTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTA CATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTC CGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTA TGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCT TTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTA TGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACC GCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCT TCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCG ATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCA CCAGCGTTTCTGGGTGAGCAAAACAGGAAGGCAAAATGCCGCAAAA AAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCT TTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGG ATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGC GCACATTTCCCCGAAAAGTGCCACCT

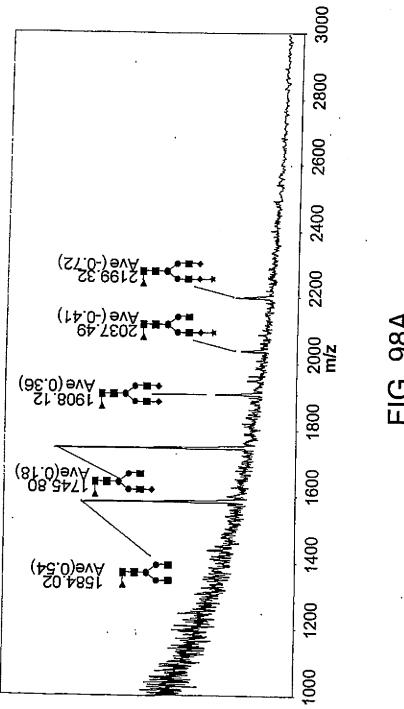


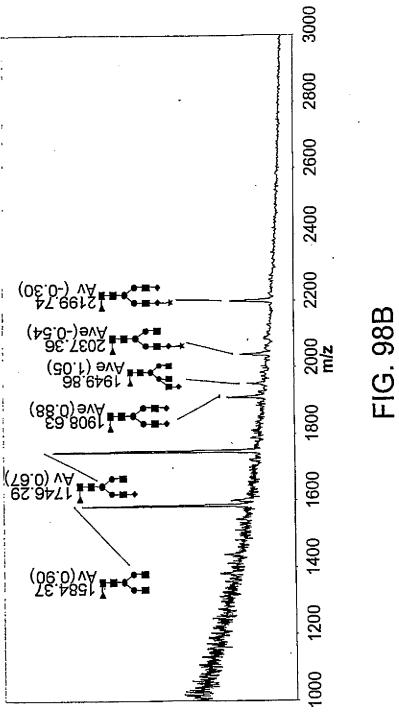


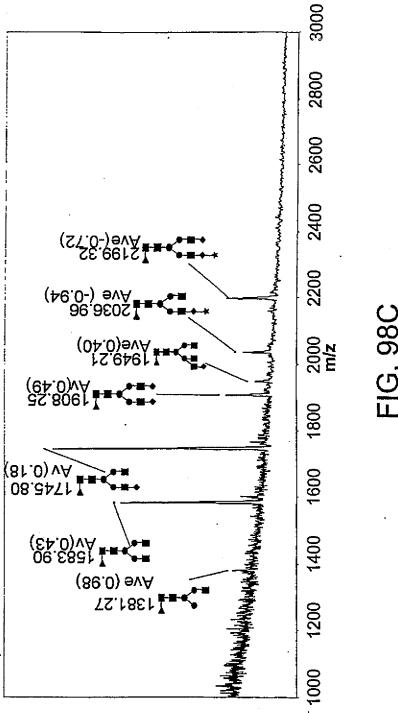


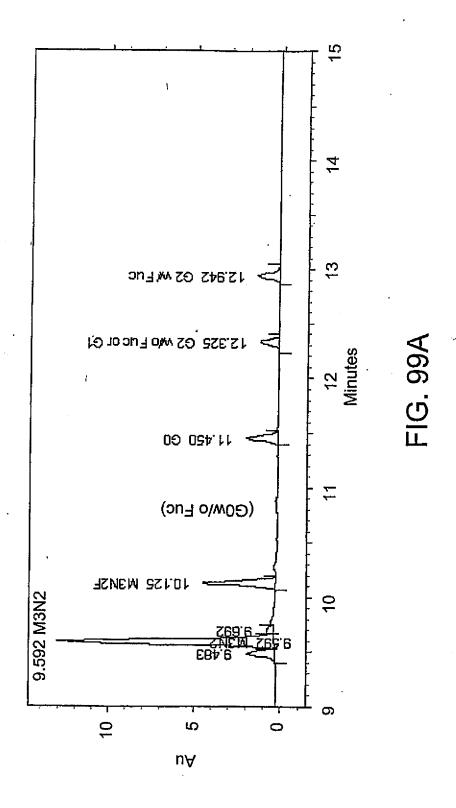


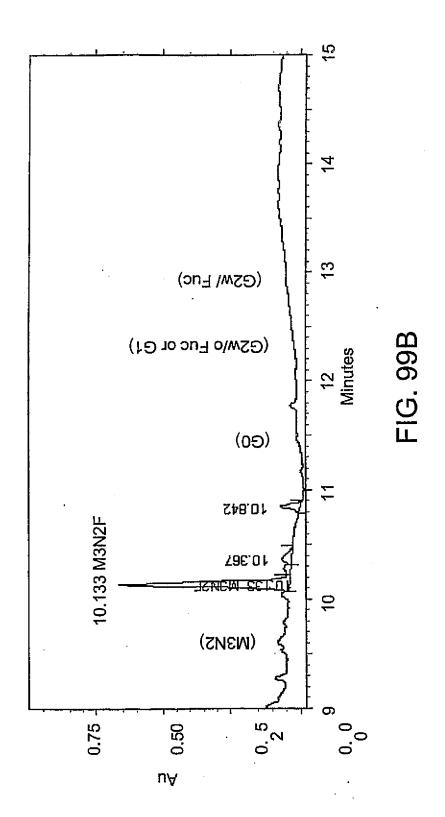
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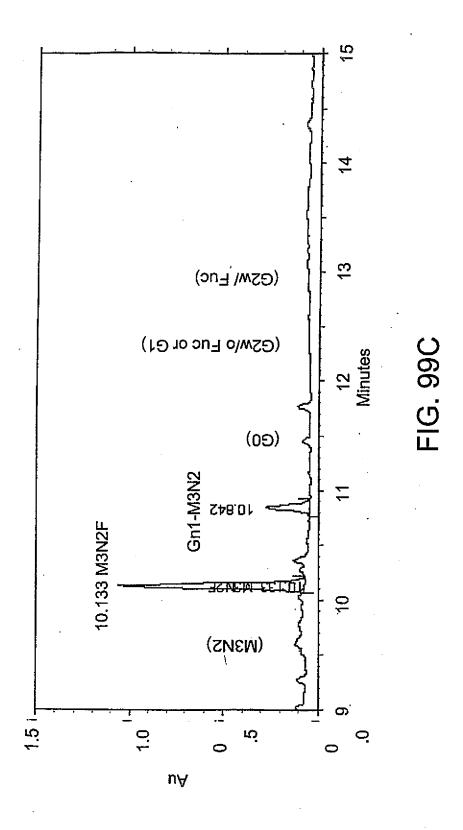




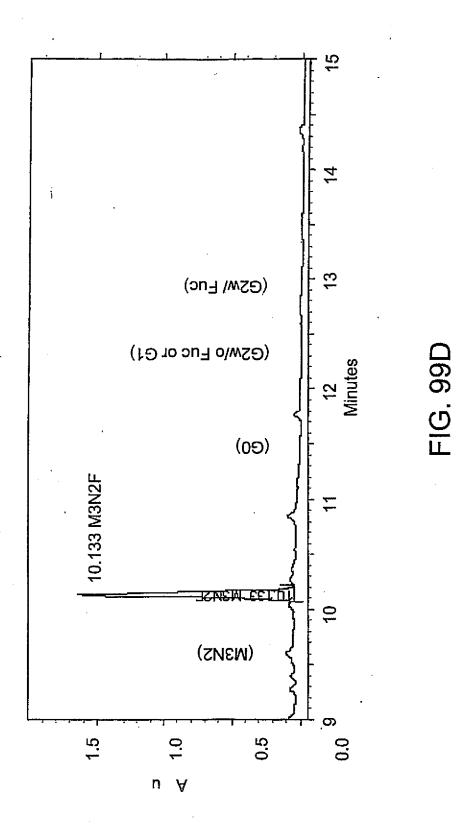


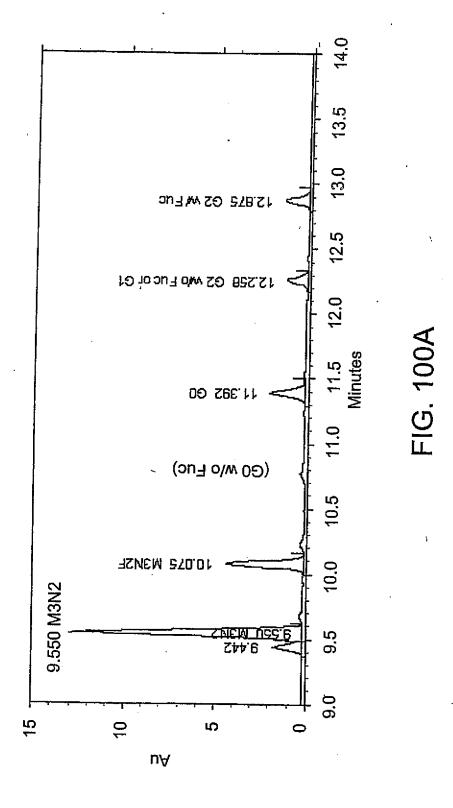


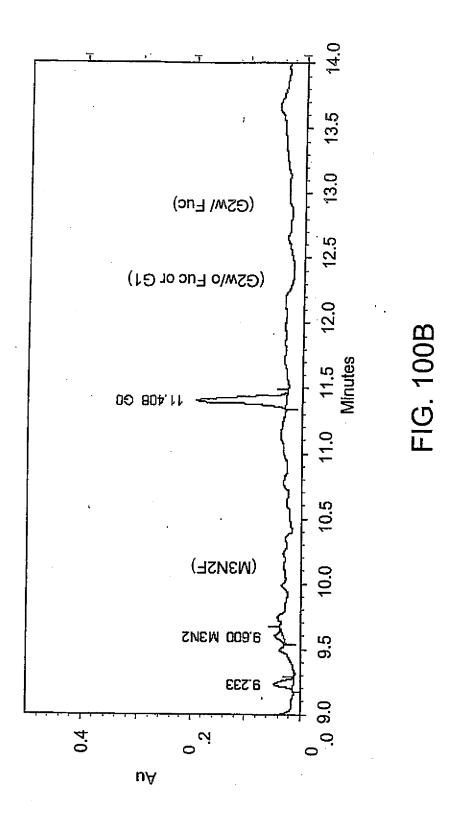
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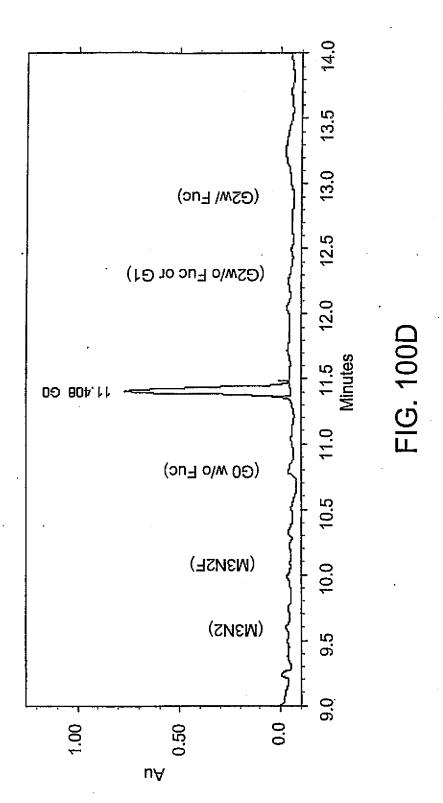


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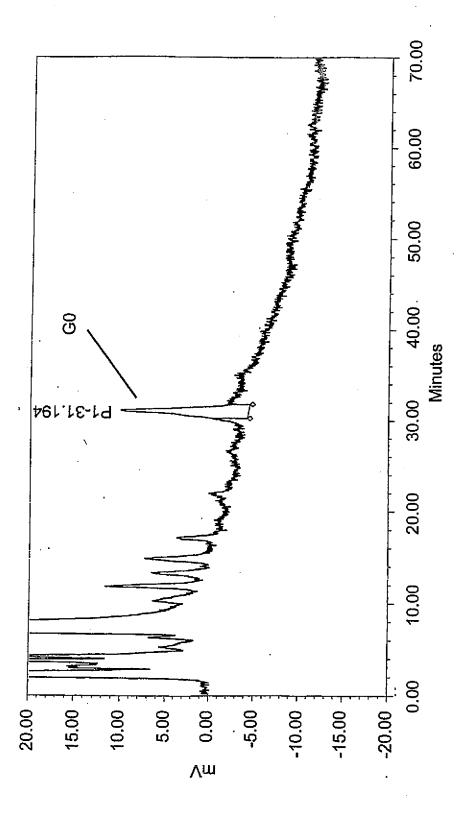


FIG. 101A

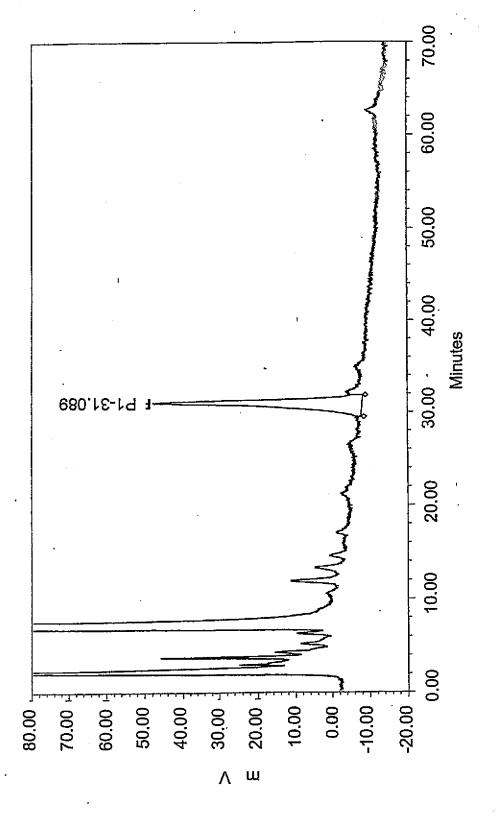
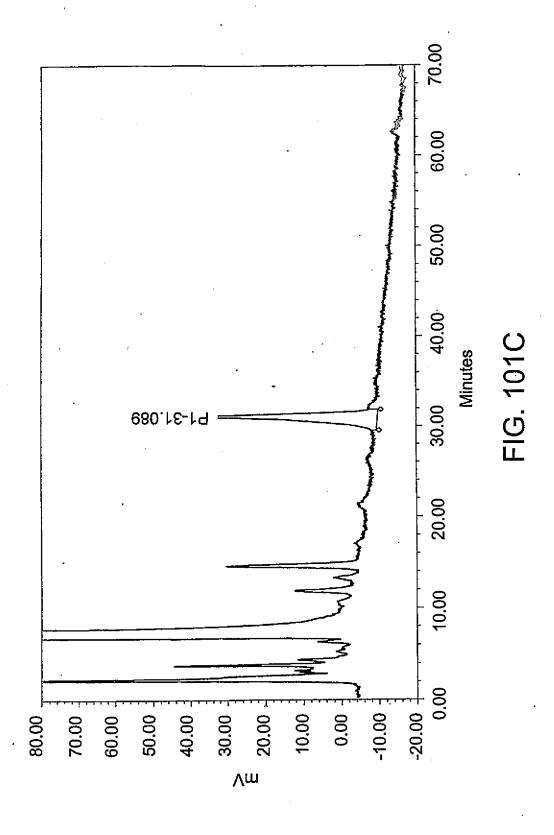


FIG. 101B

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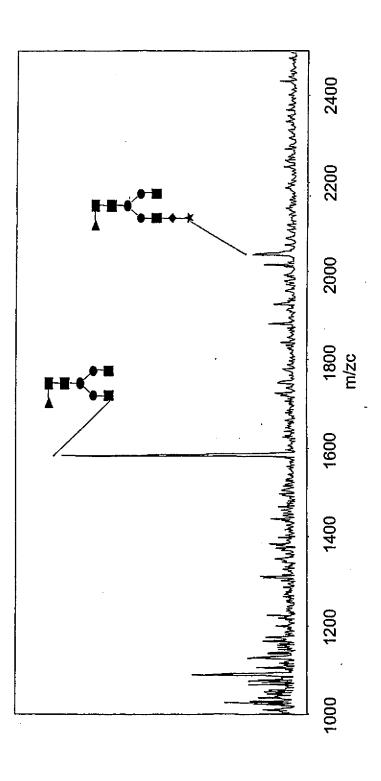
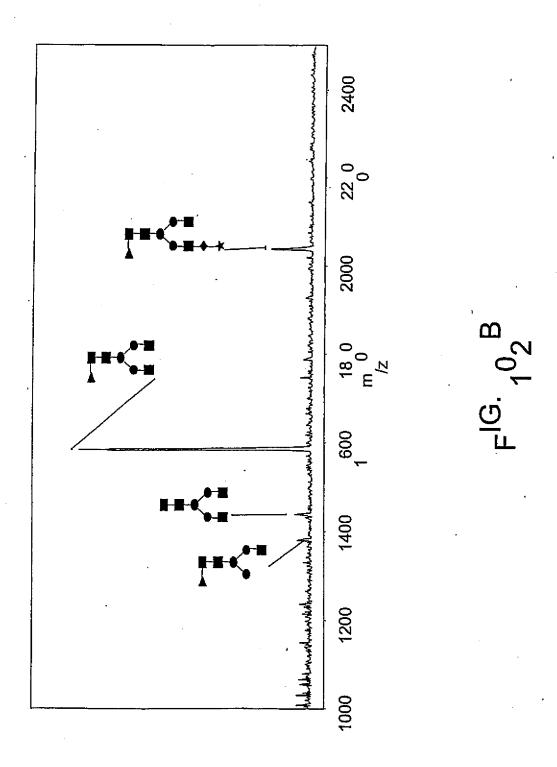


FIG. 102A

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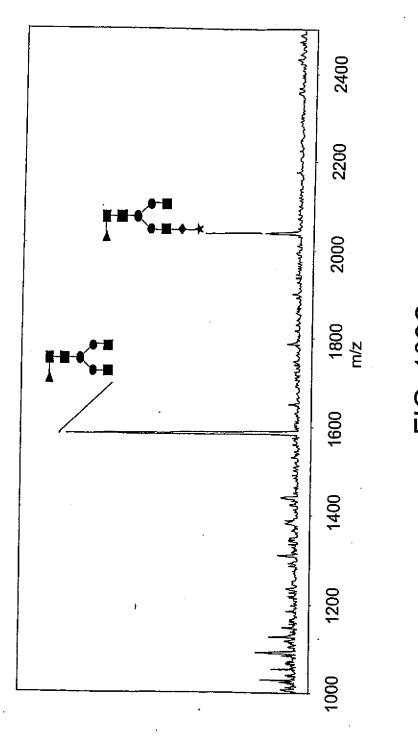
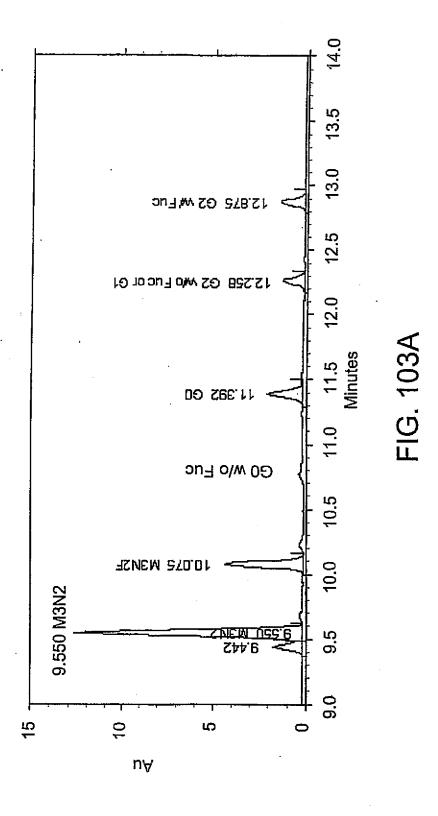
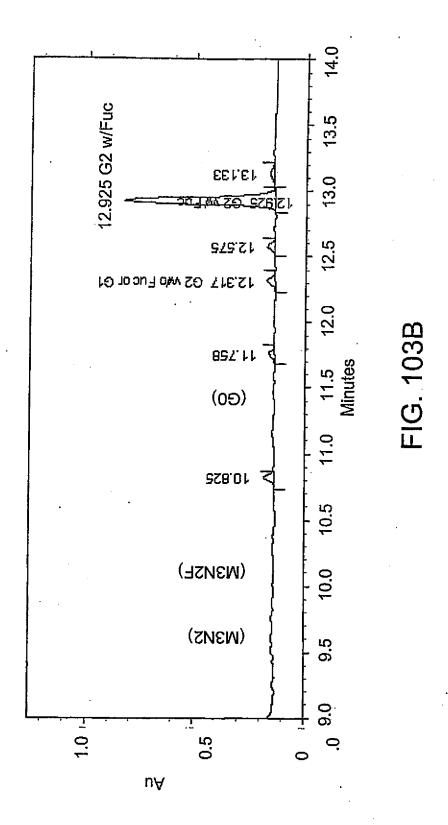
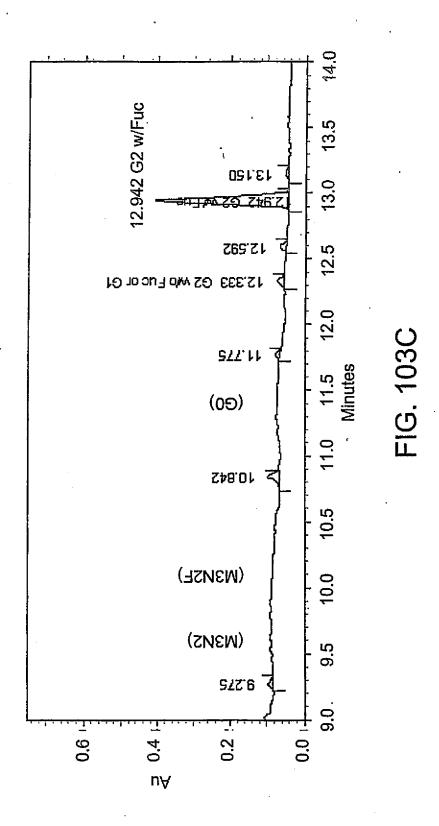


FIG. 102C







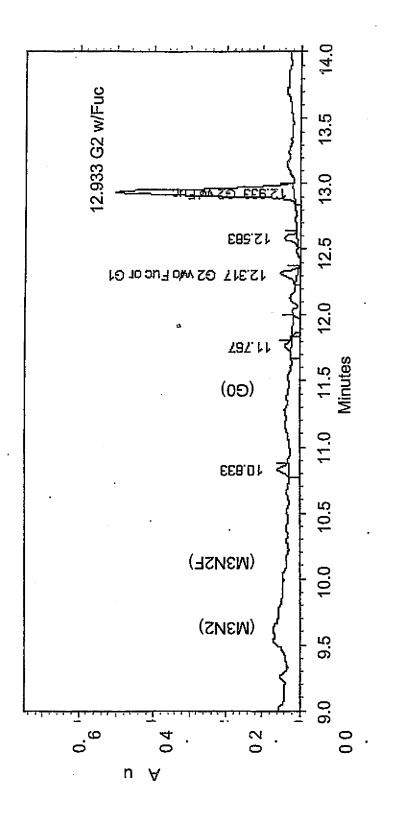
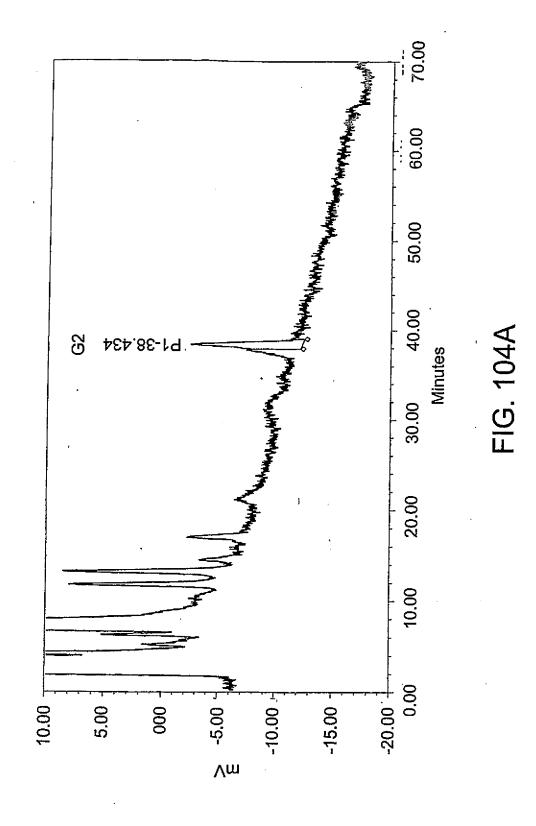


FIG. 103D

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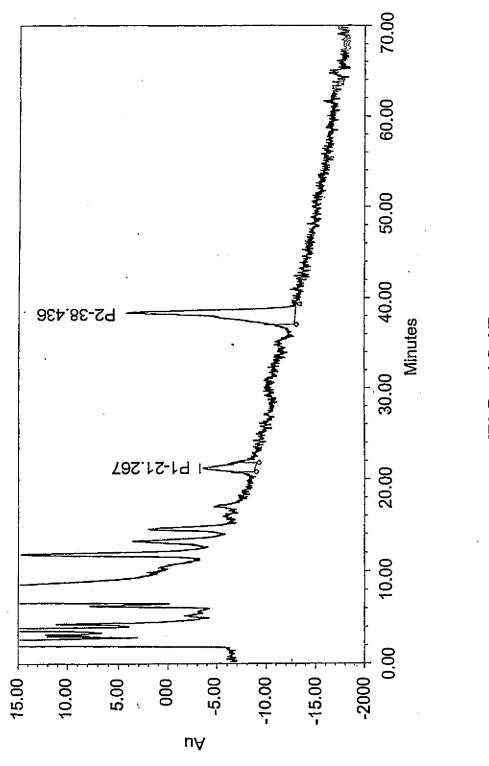
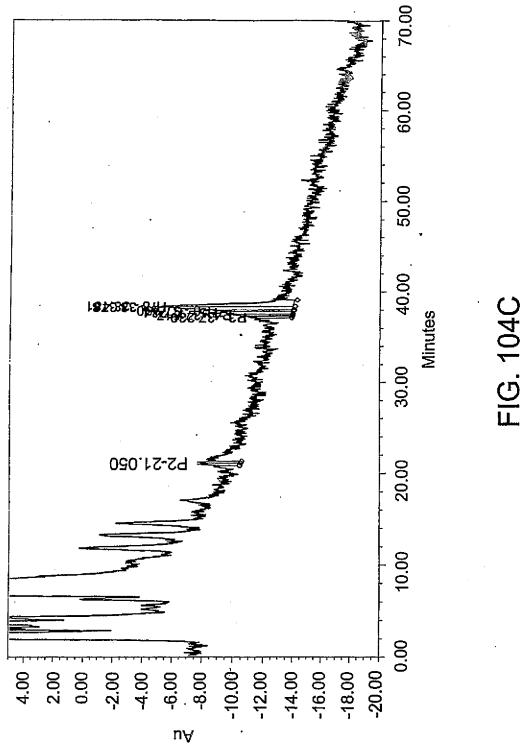
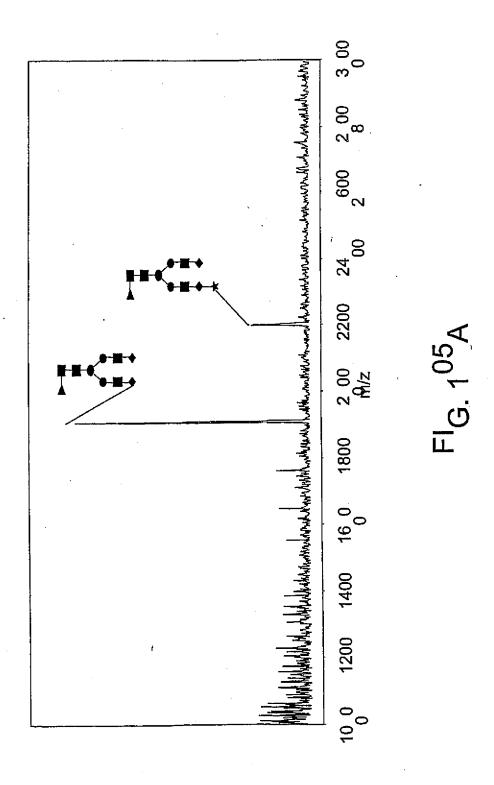


FIG. 104B



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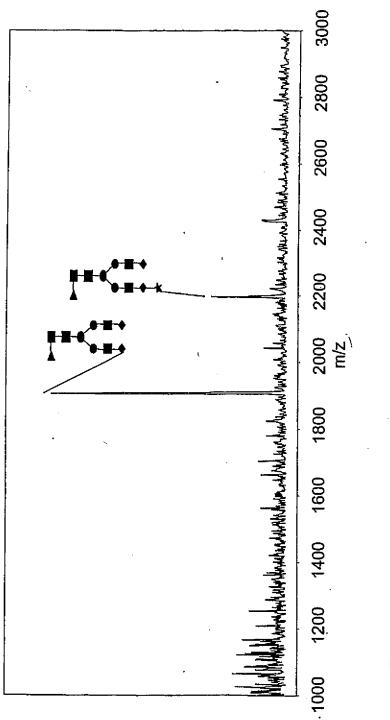


FIG. 105B

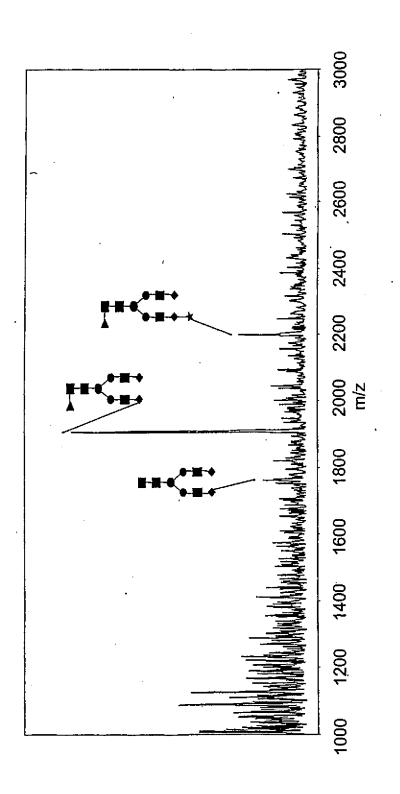
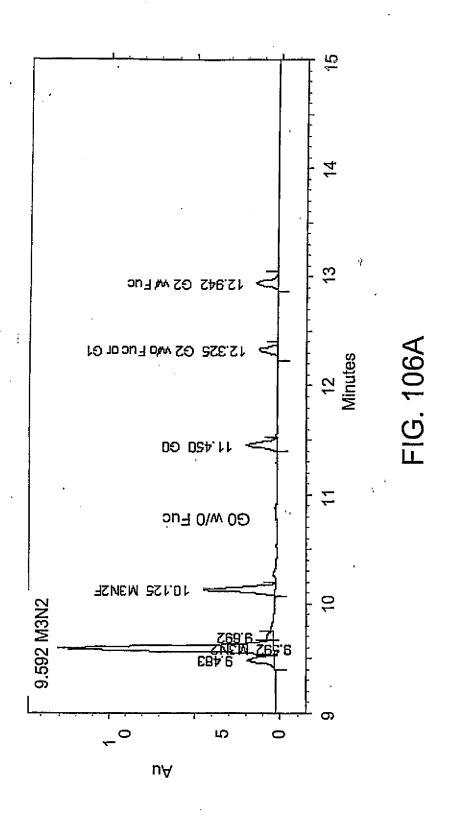
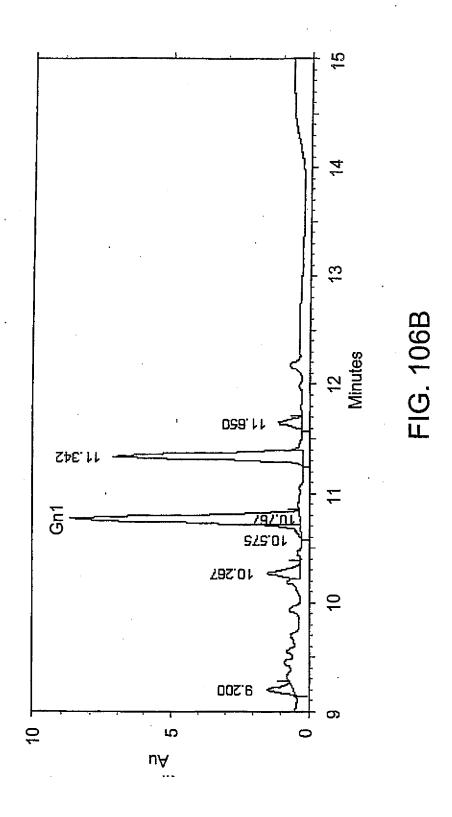
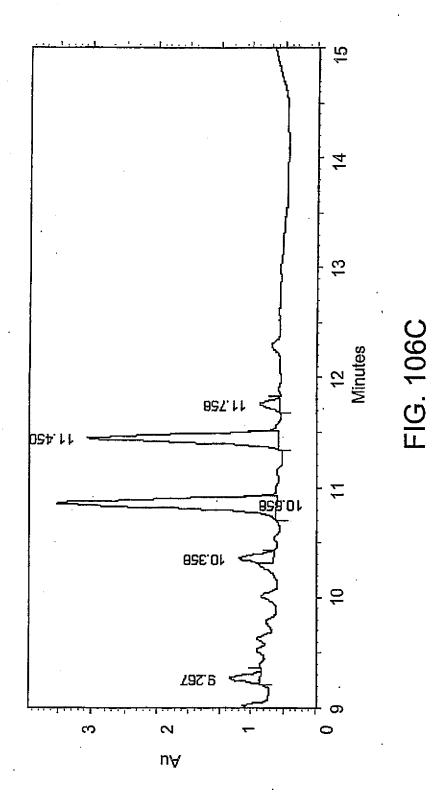
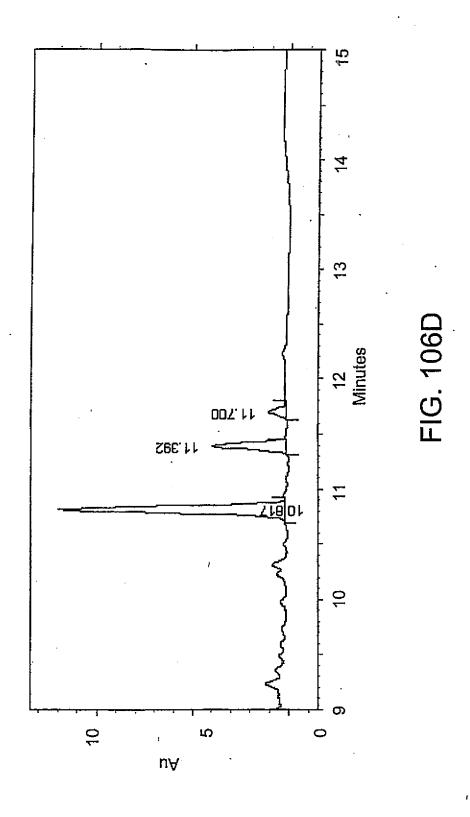


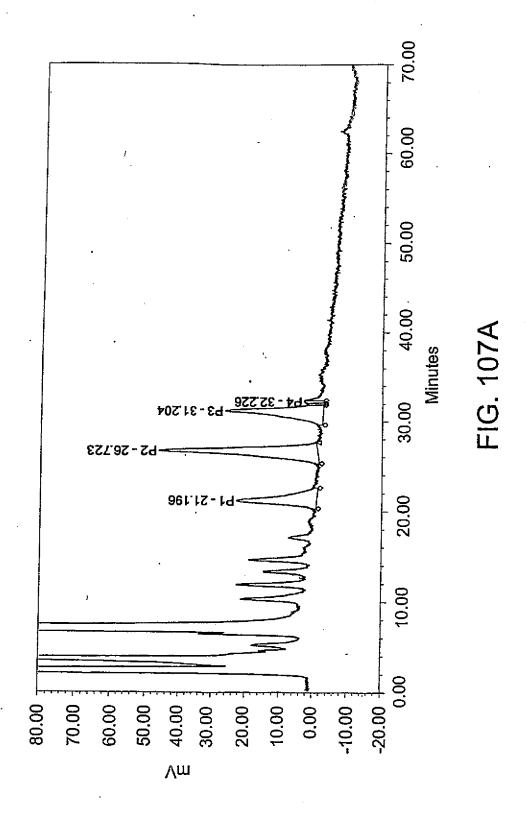
FIG. 105C

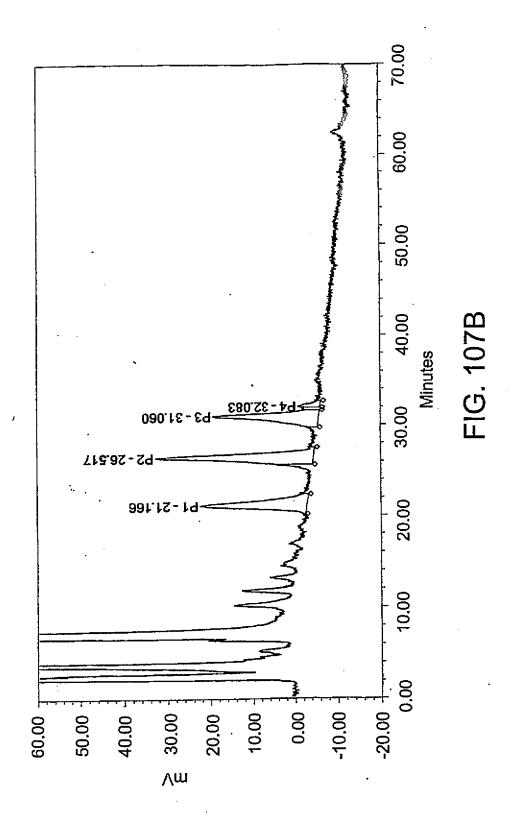




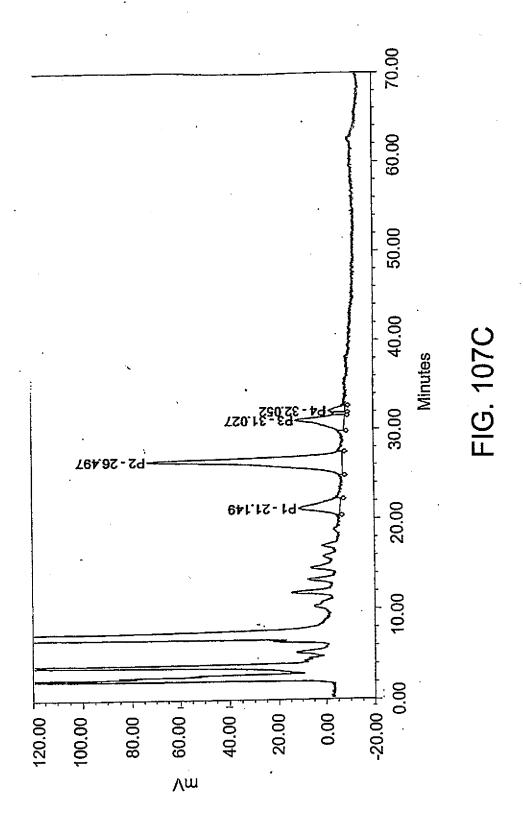


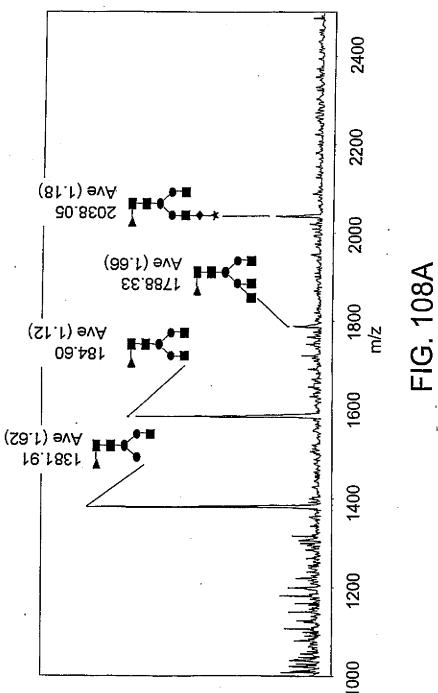


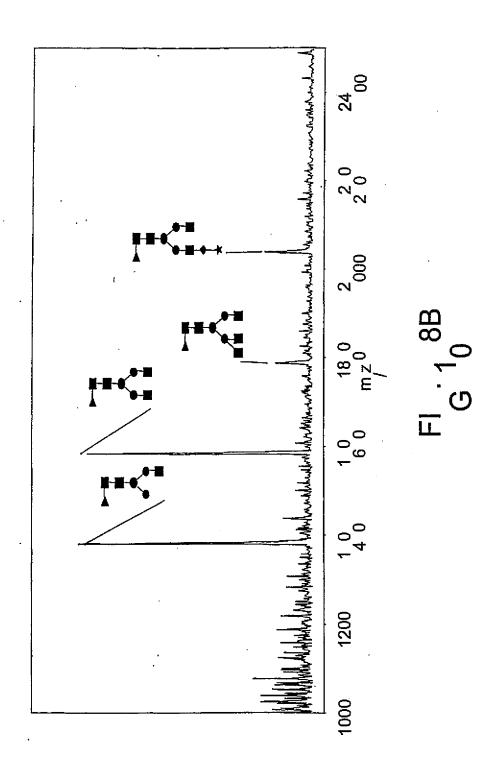


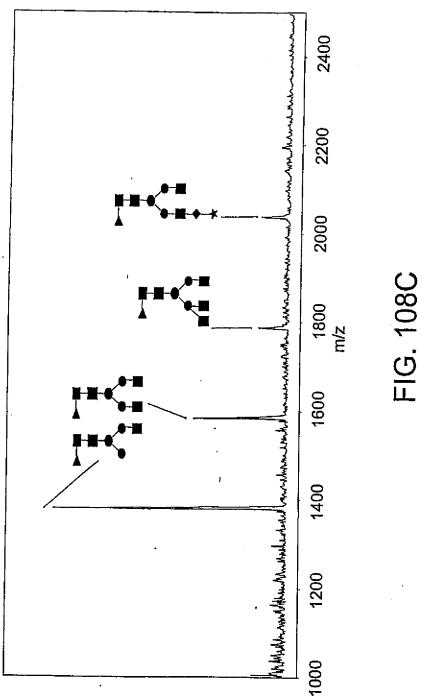


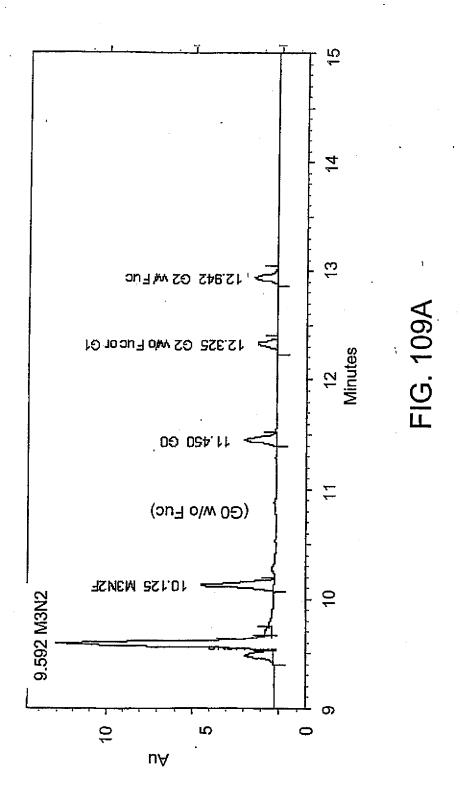
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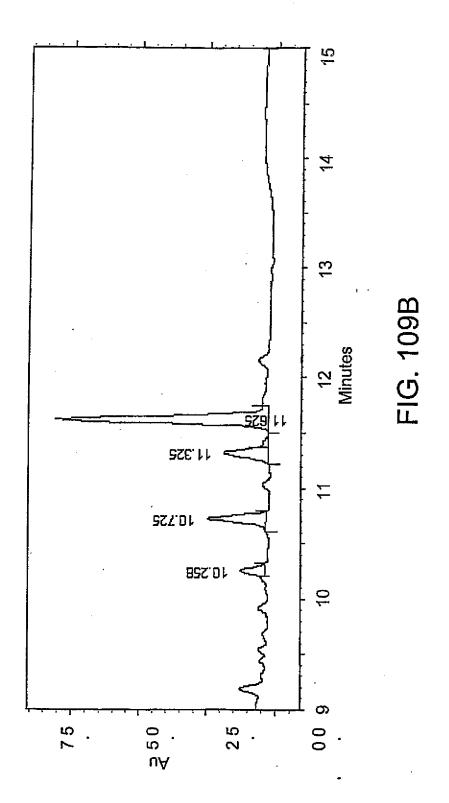




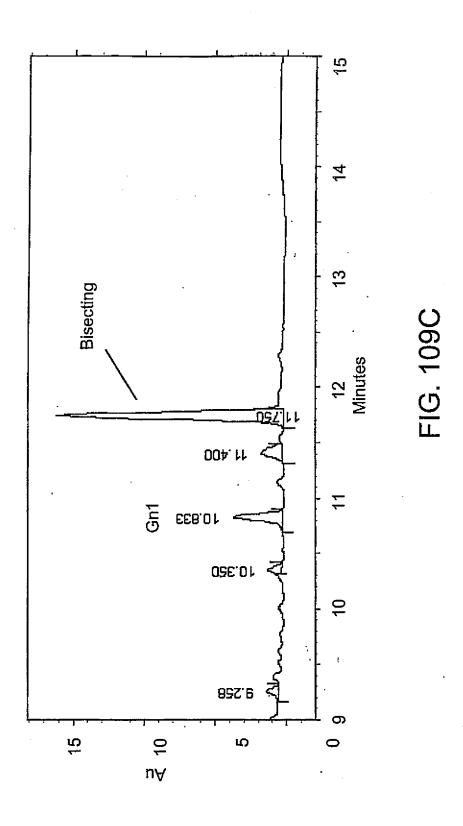




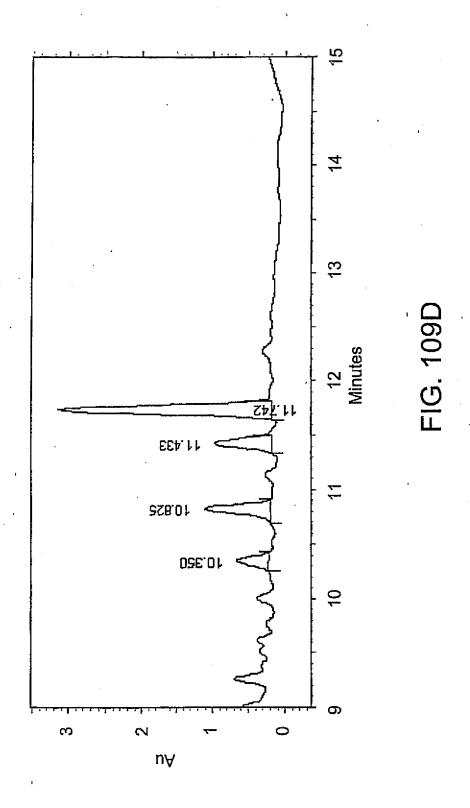


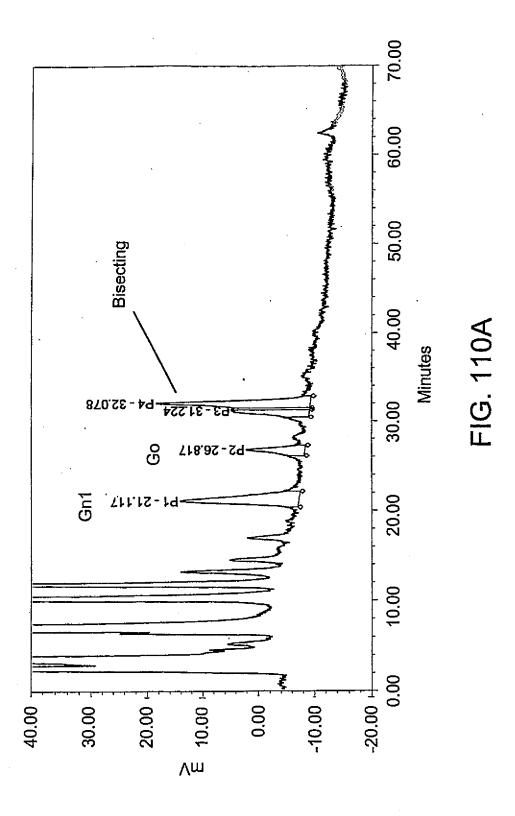


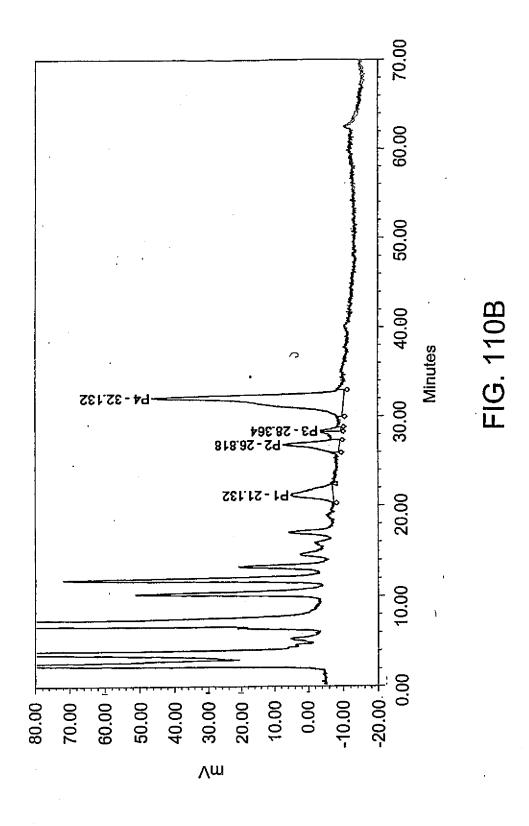
ŧ

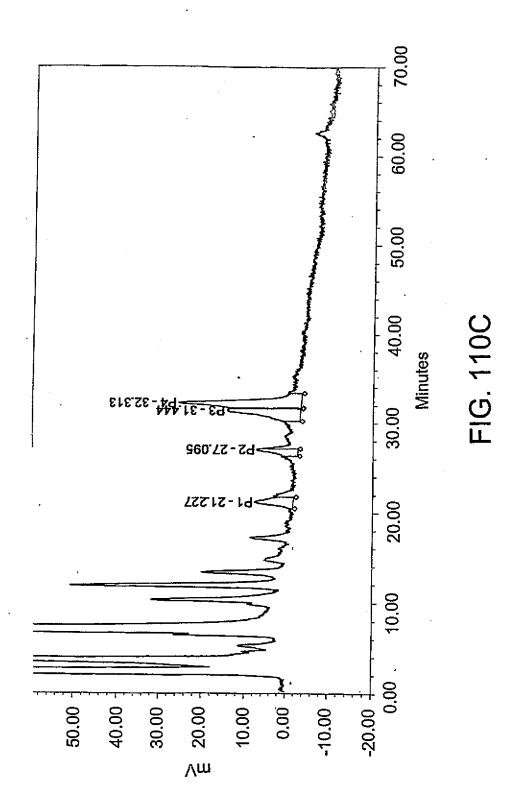


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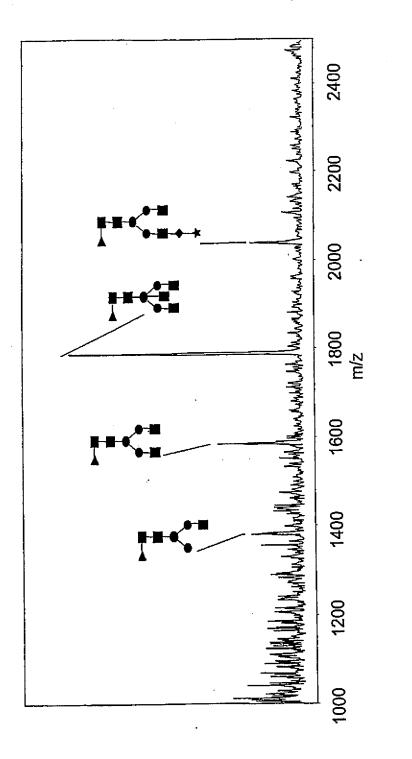


FIG. 111A

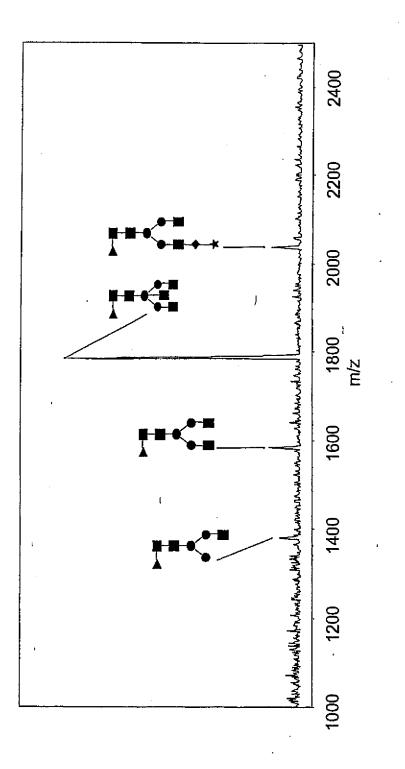
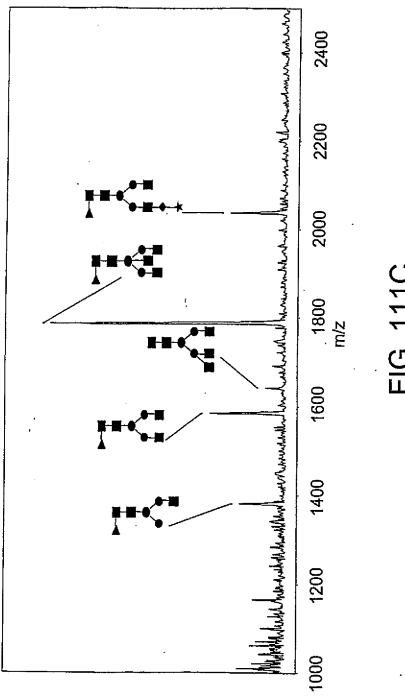


FIG. 111B



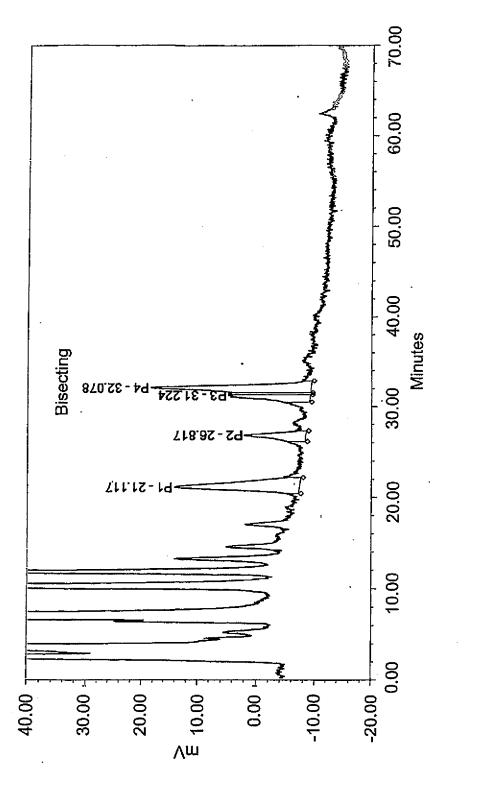
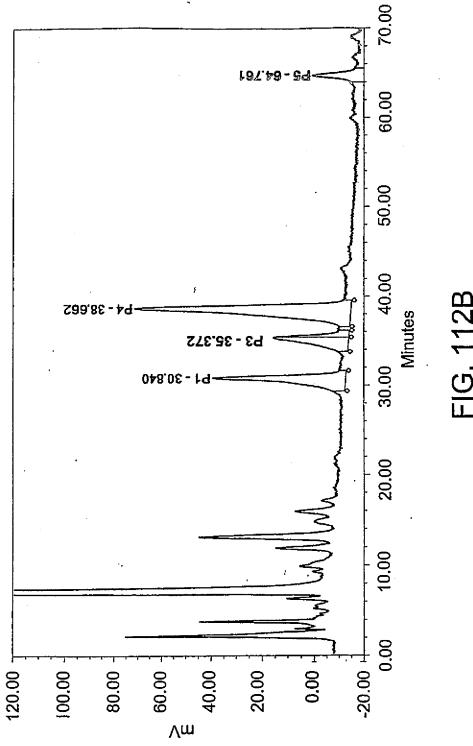
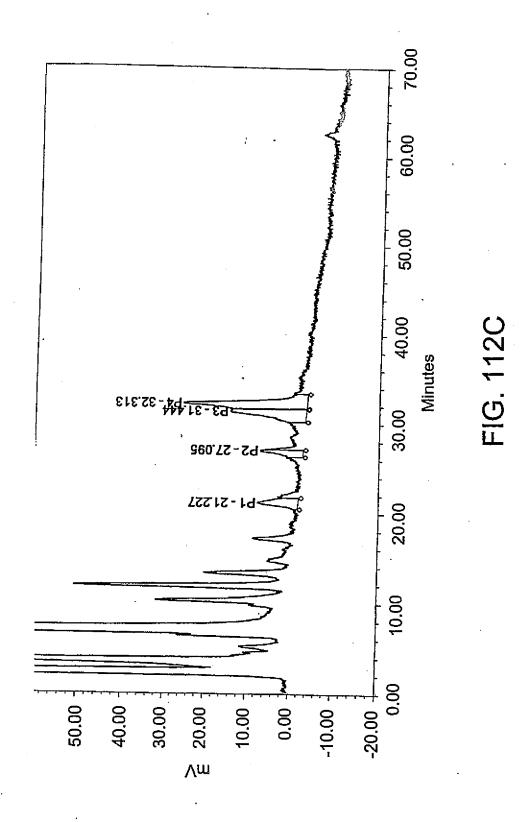
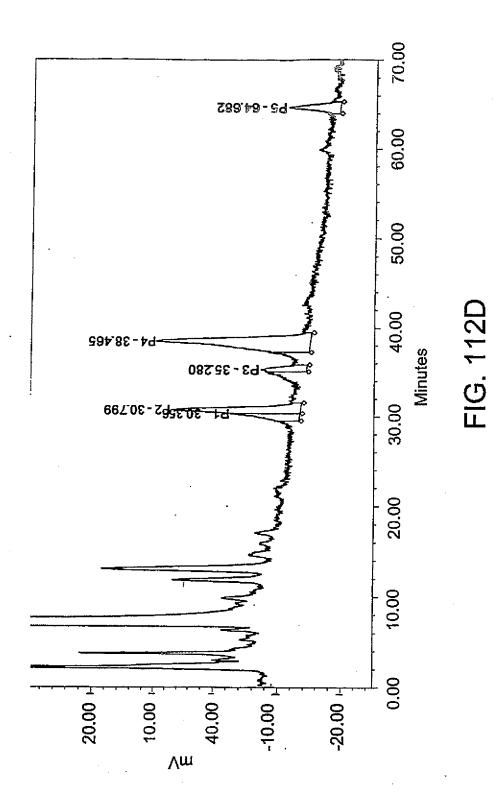


FIG. 112A

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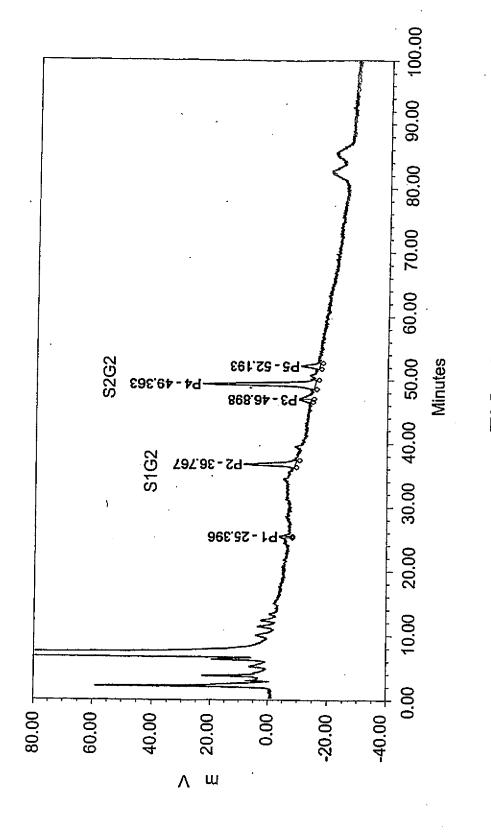
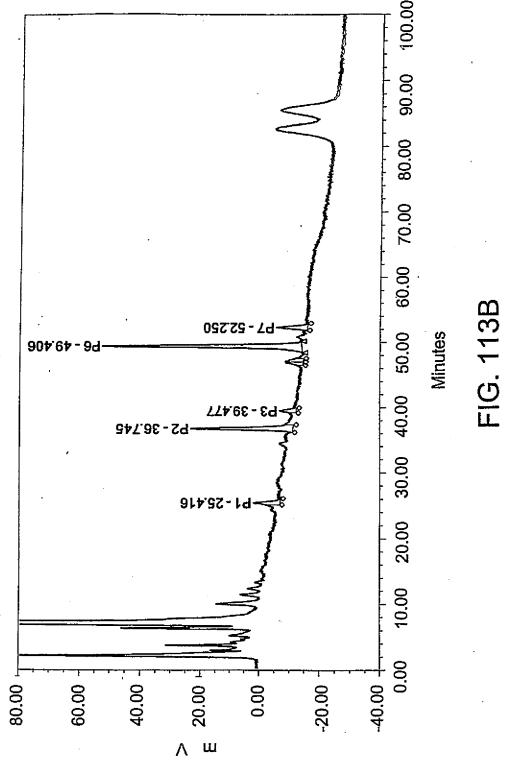
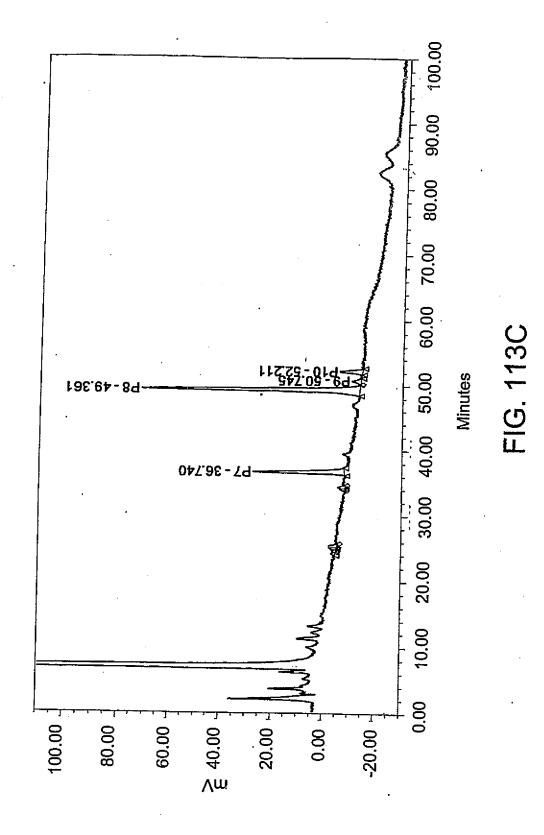
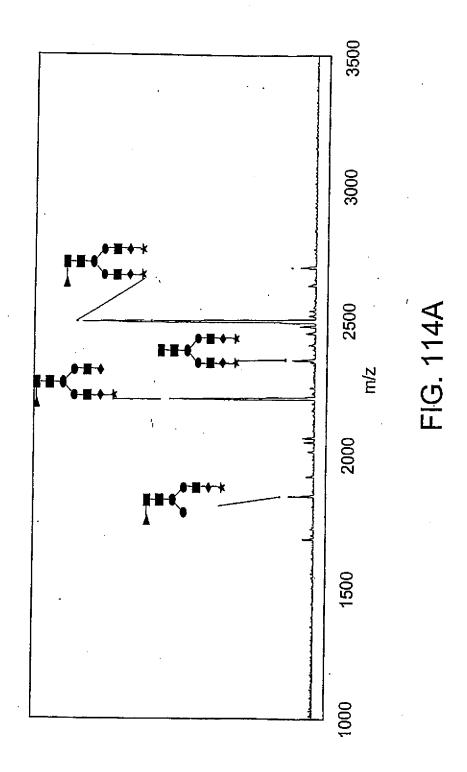
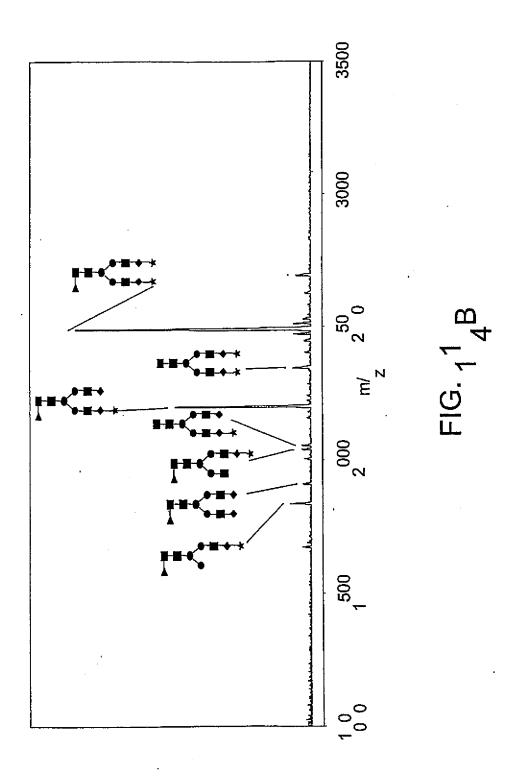


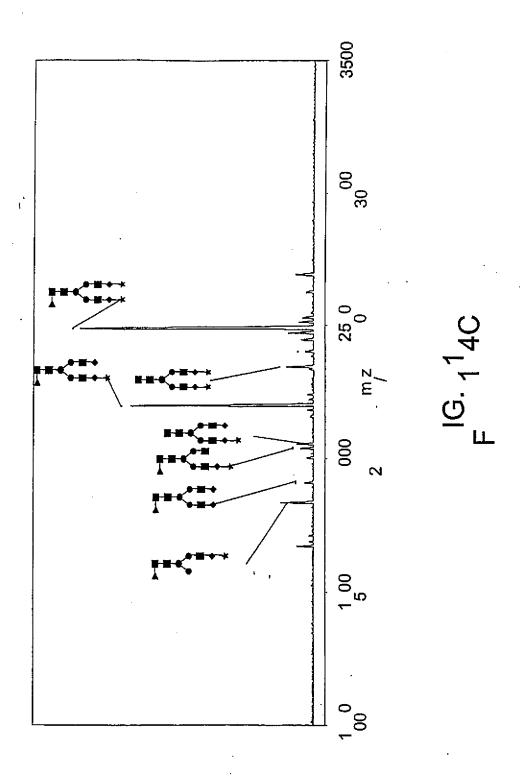
FIG. 113A











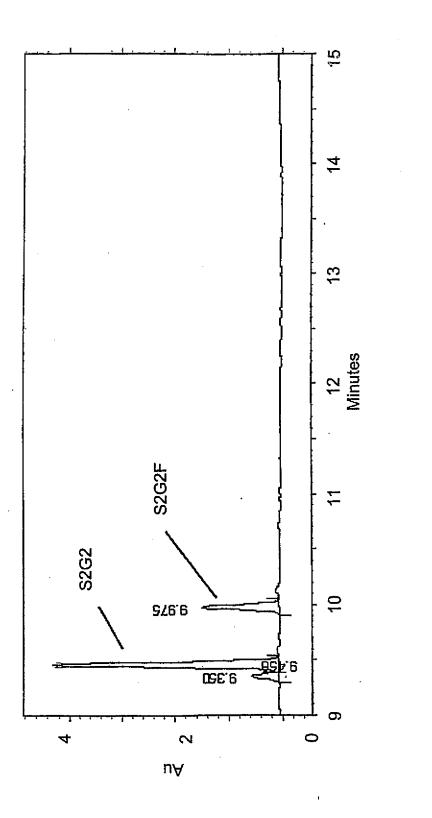
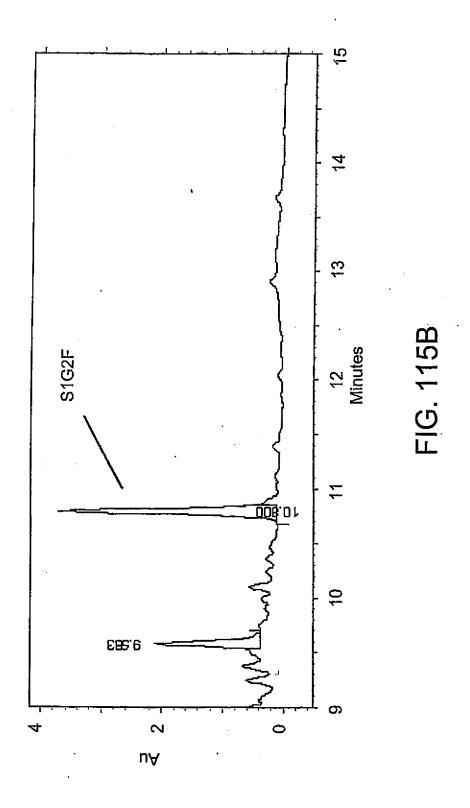
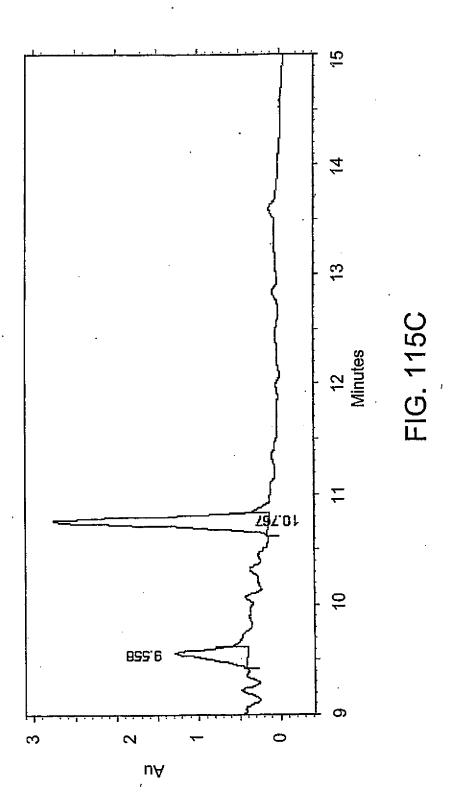
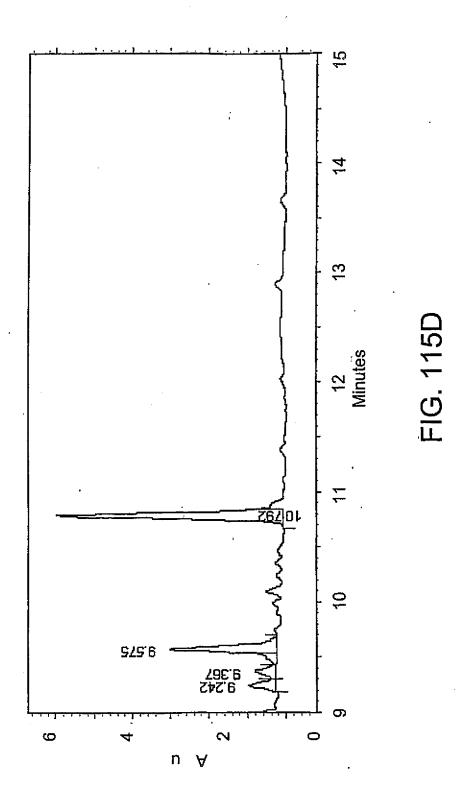


FIG. 115A







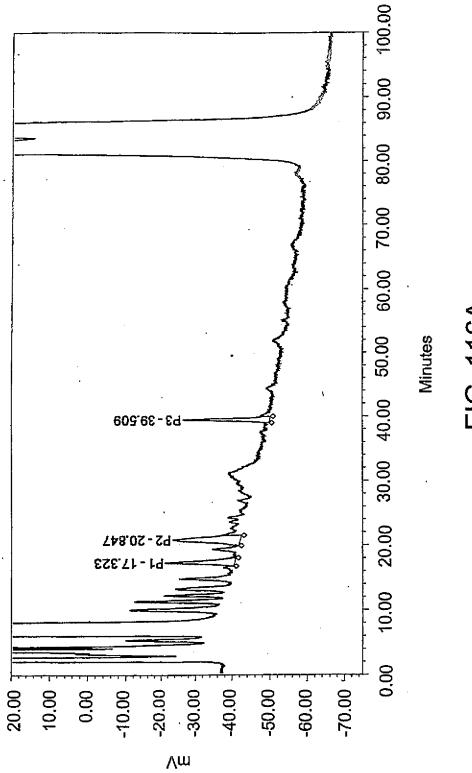
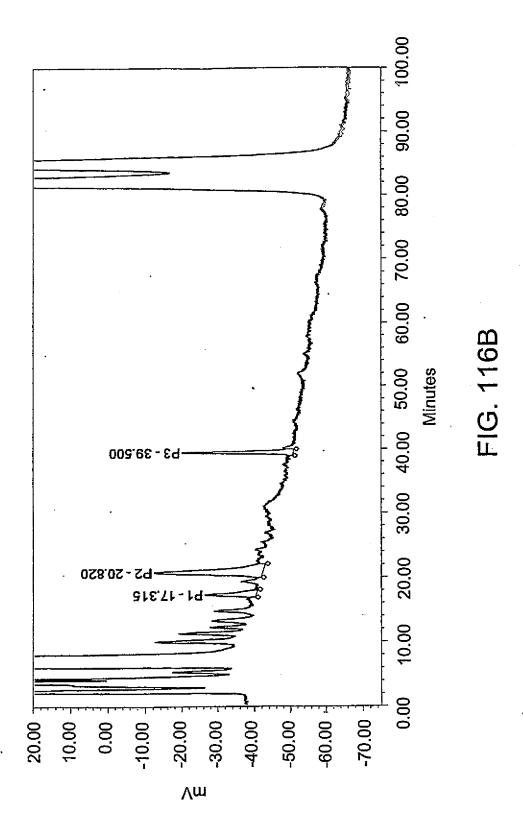
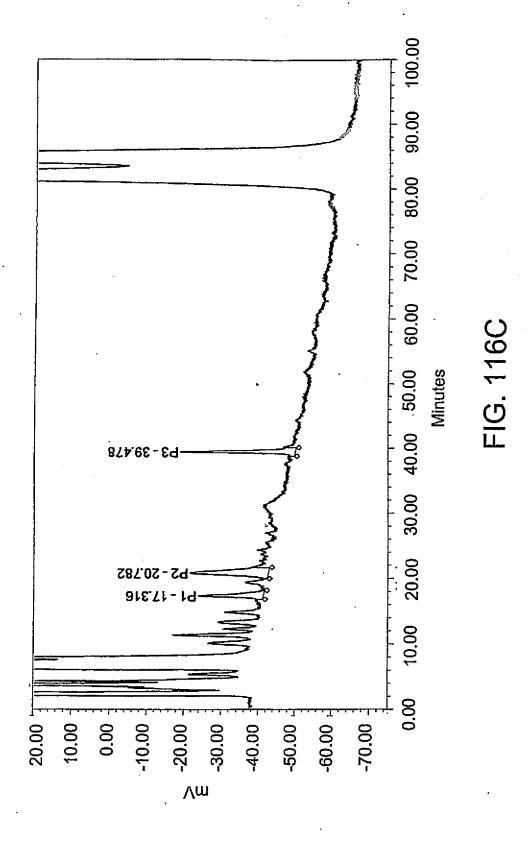
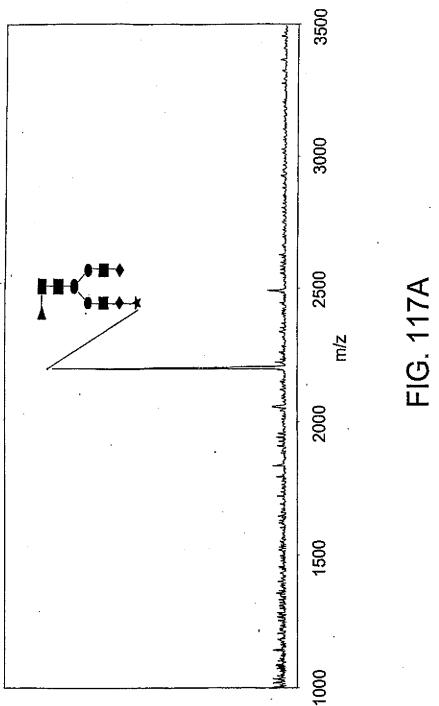
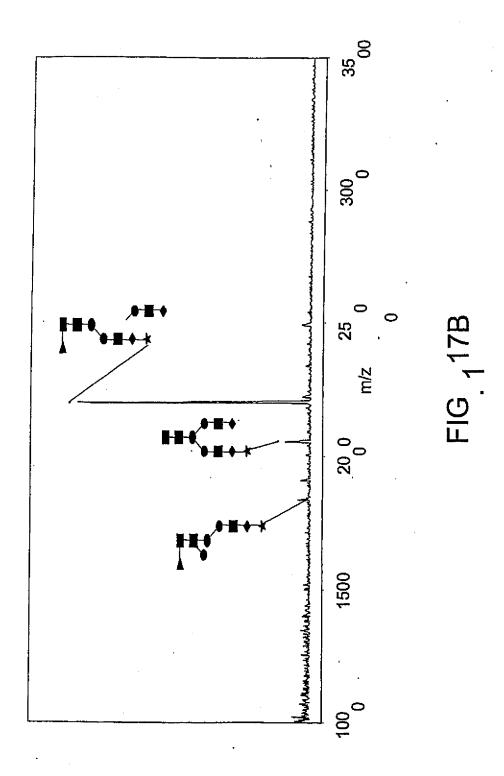


FIG. 116A









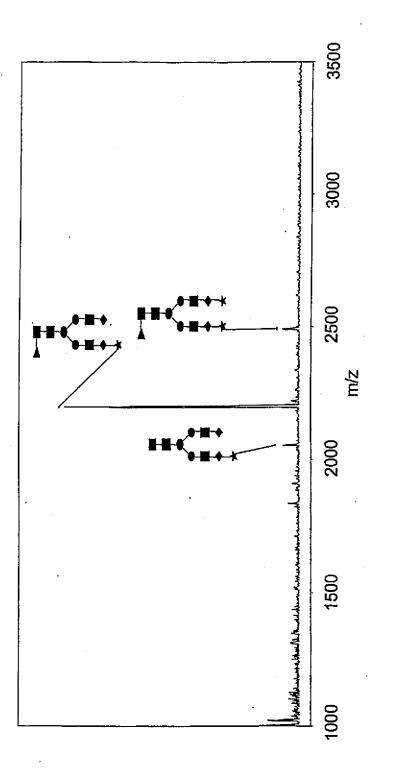


FIG. 117C

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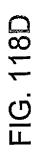
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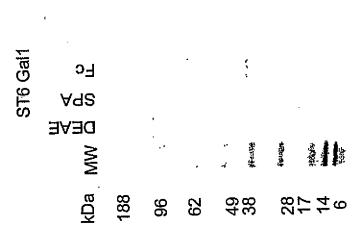
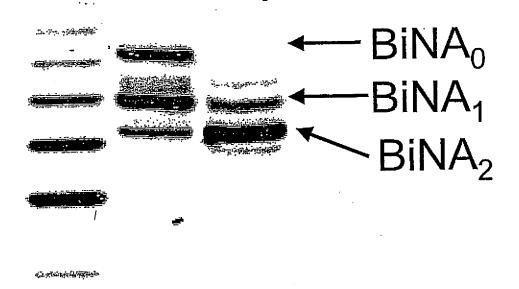
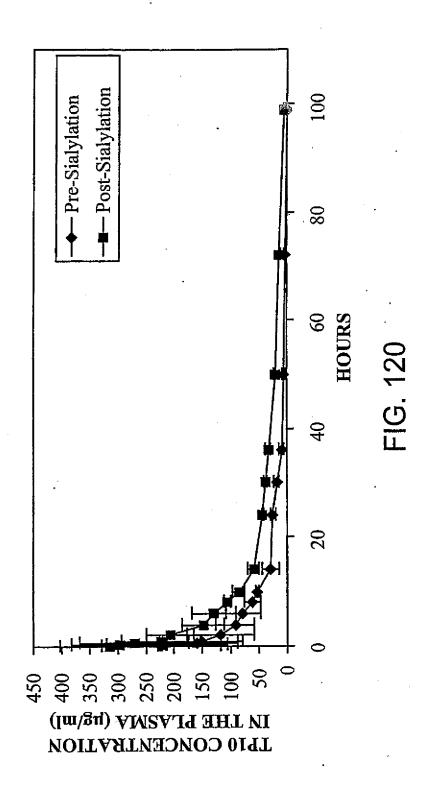


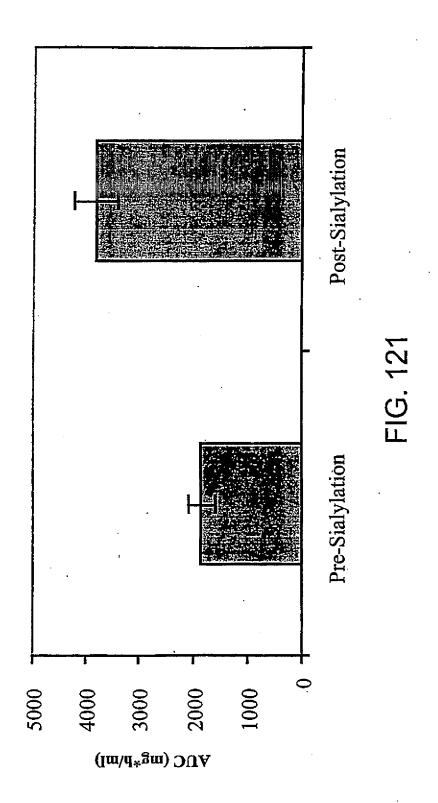
FIG. 118C

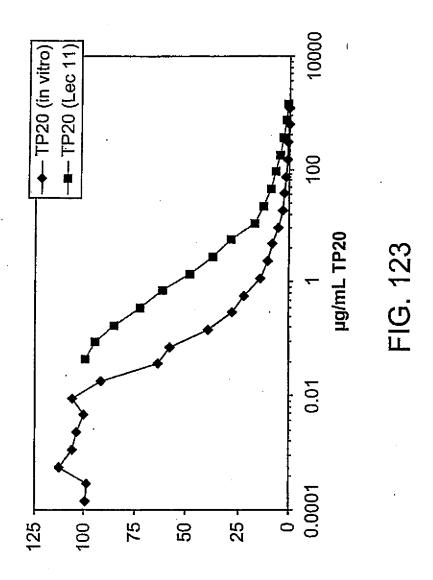


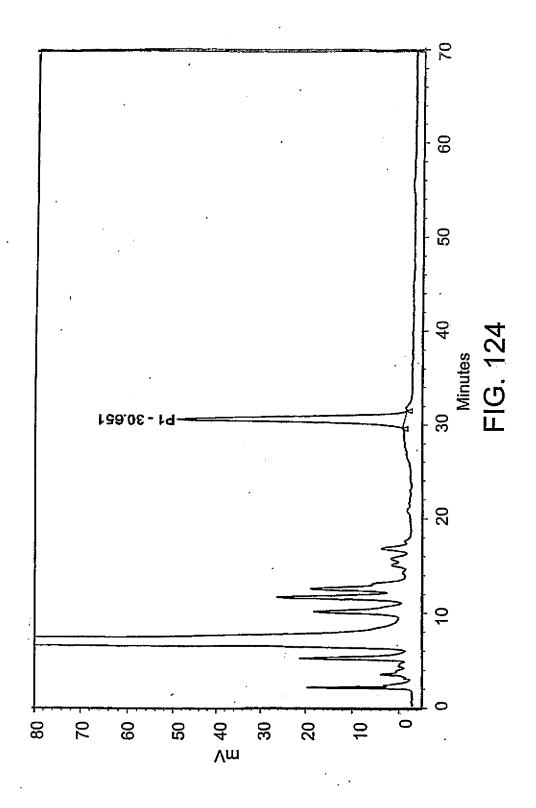
Pre Post

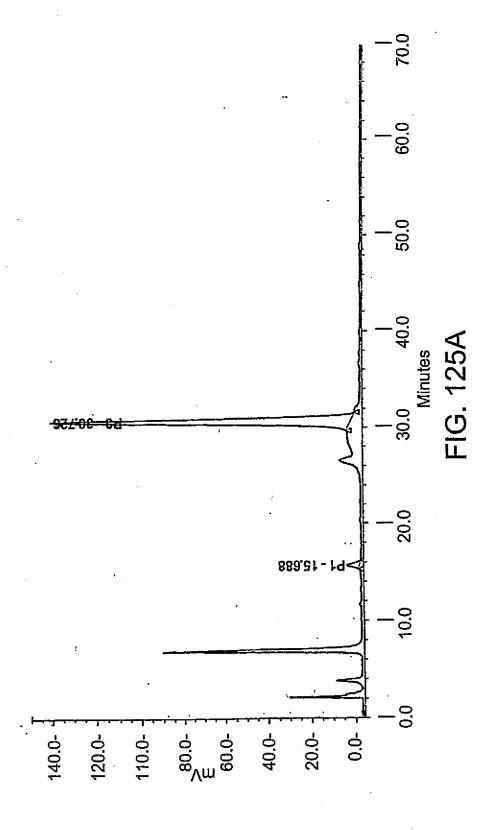
FIG. 119

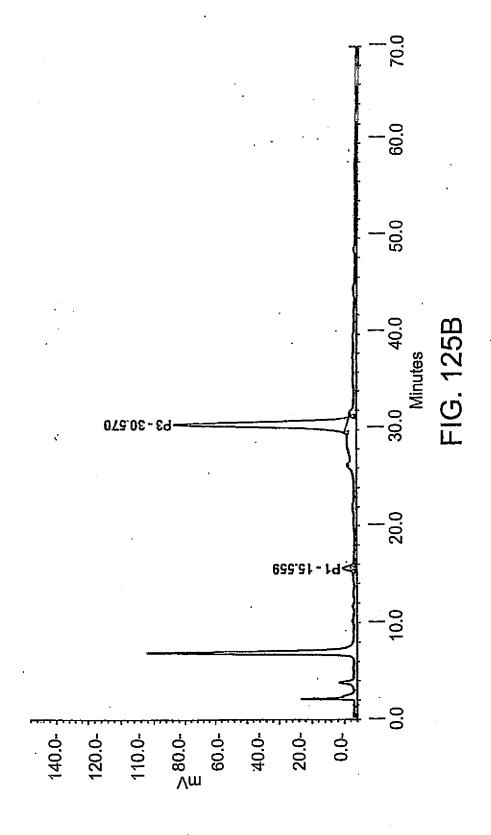


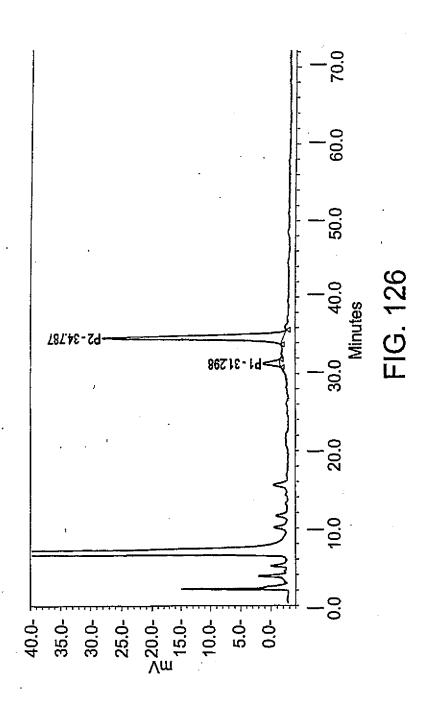


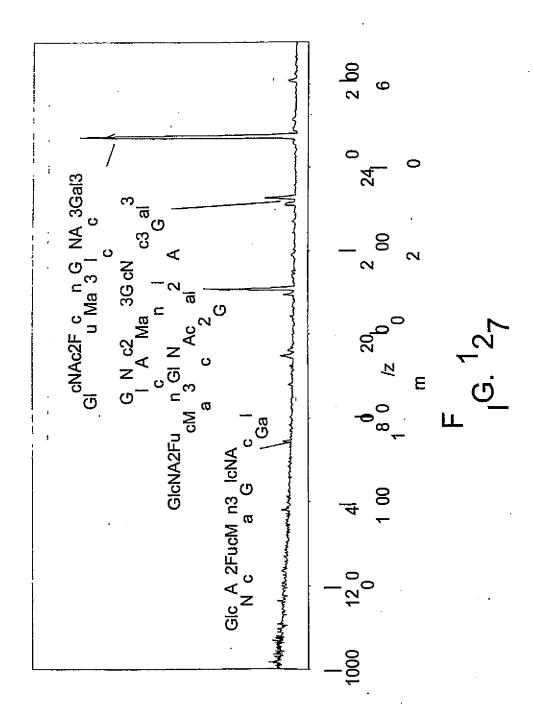


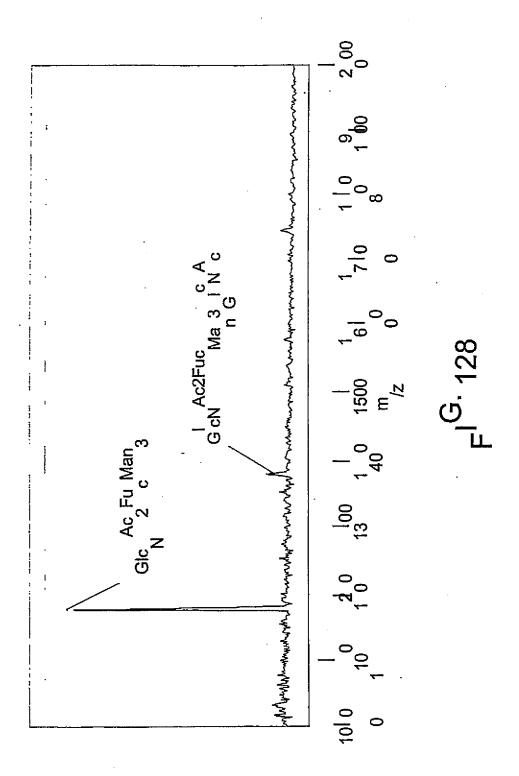












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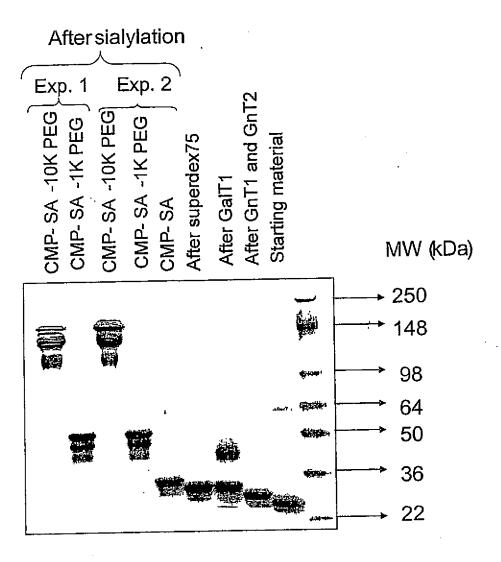
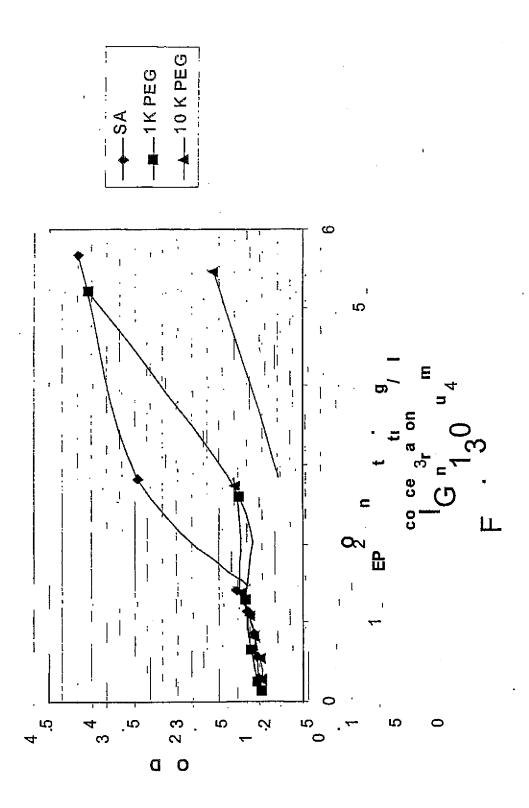
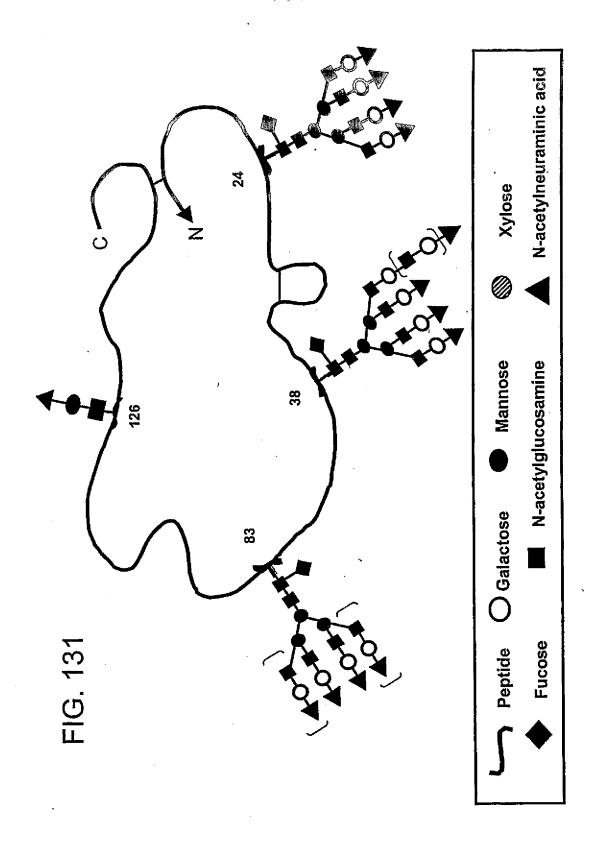


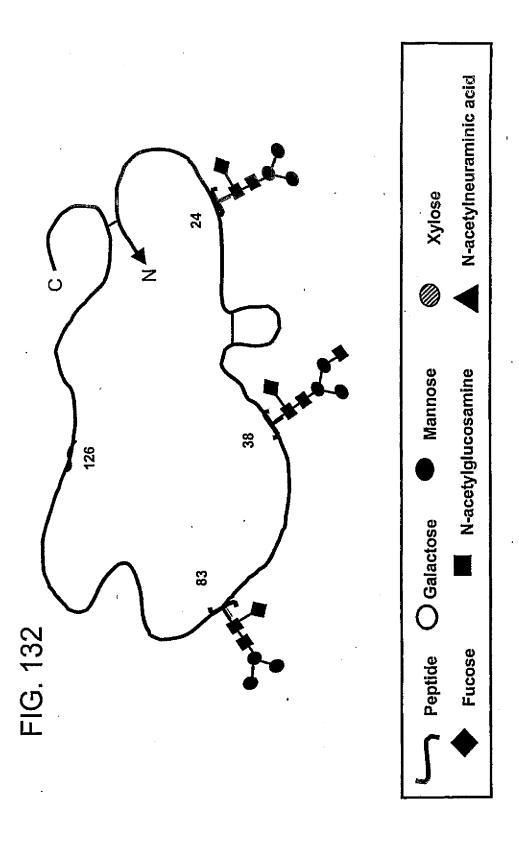
FIG. 129

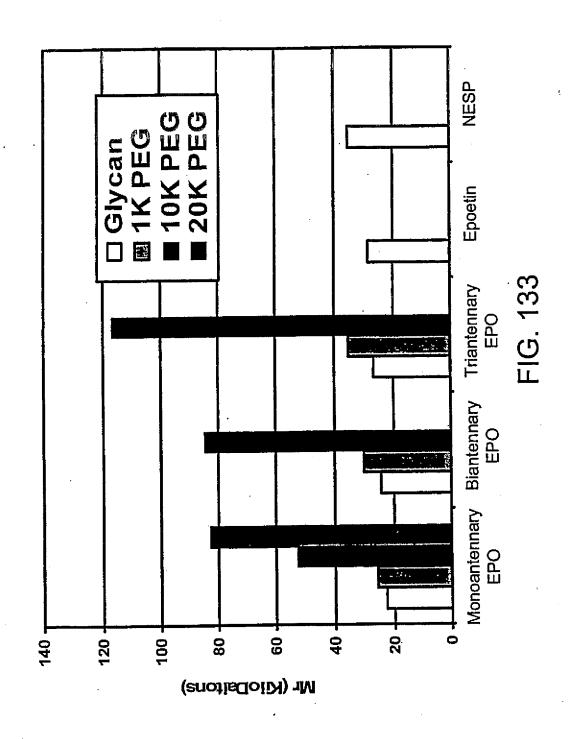


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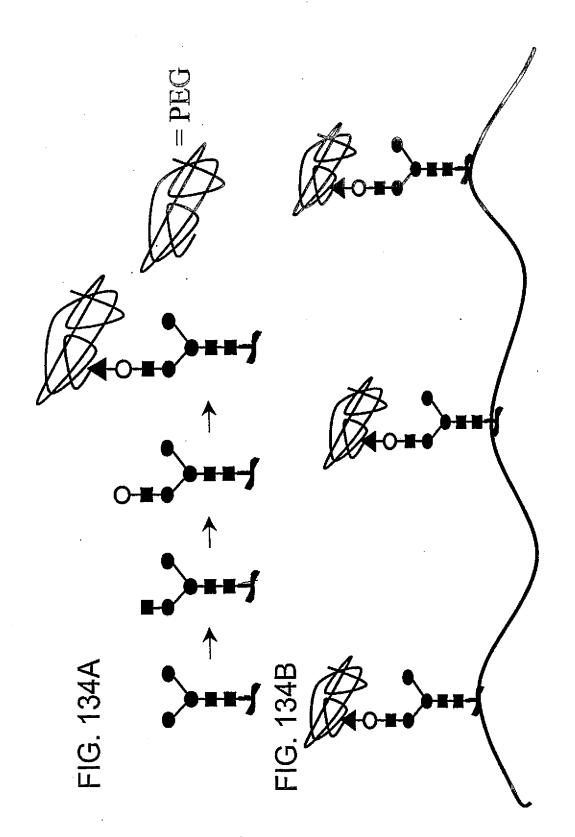


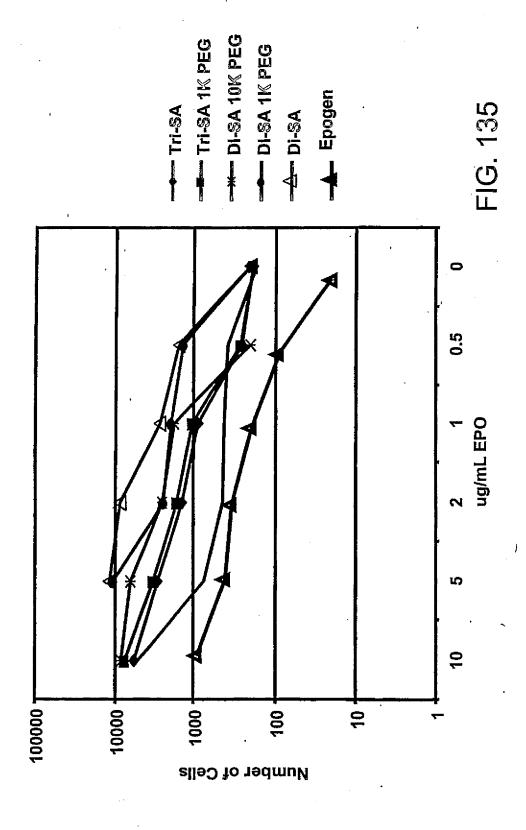
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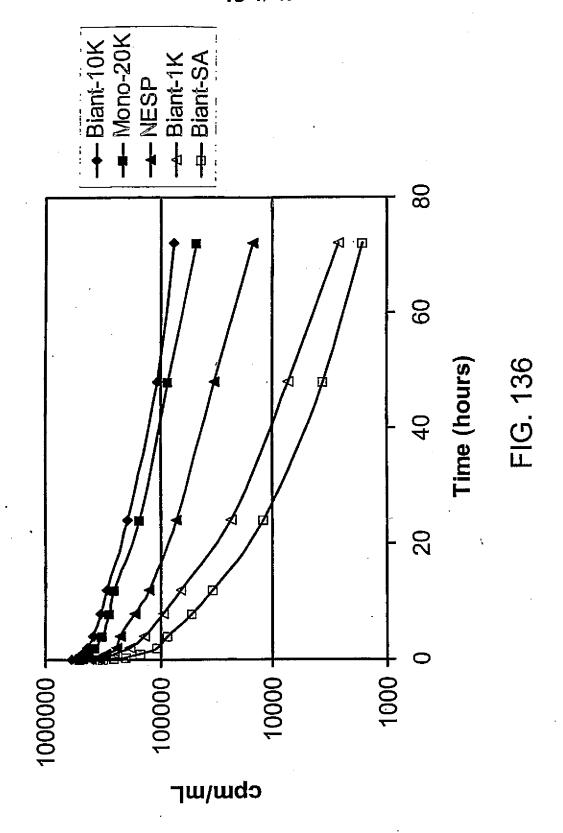


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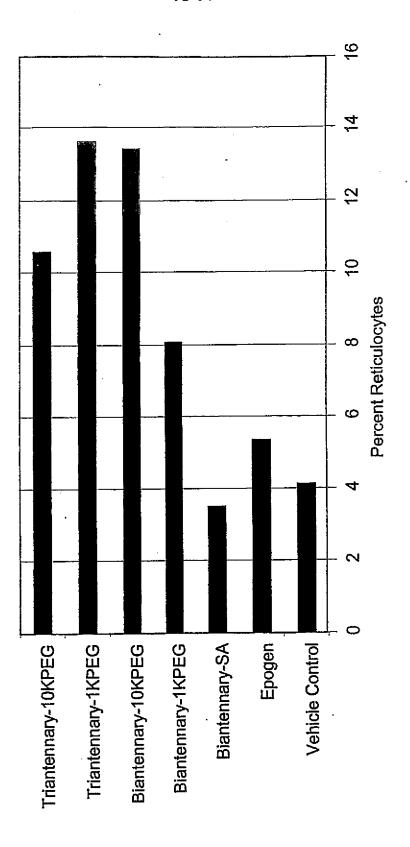


FIG. 137

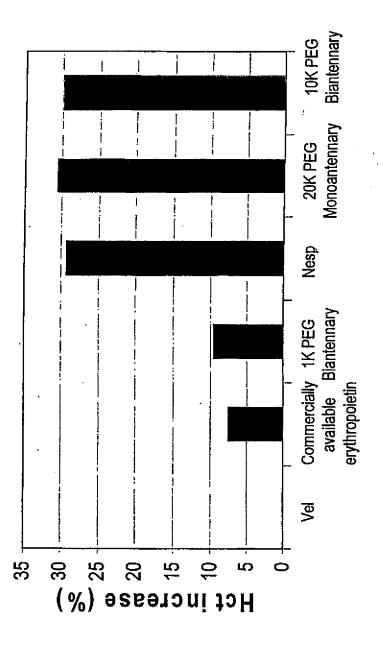
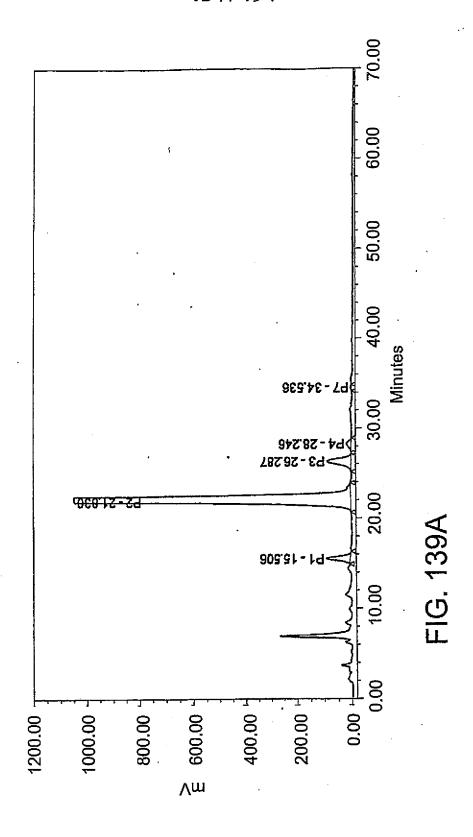
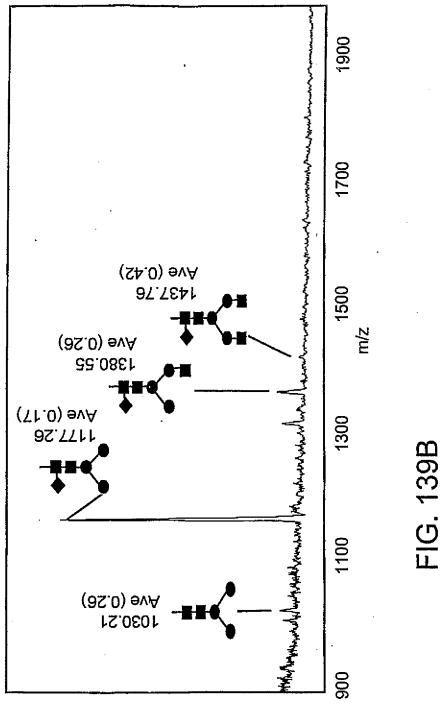
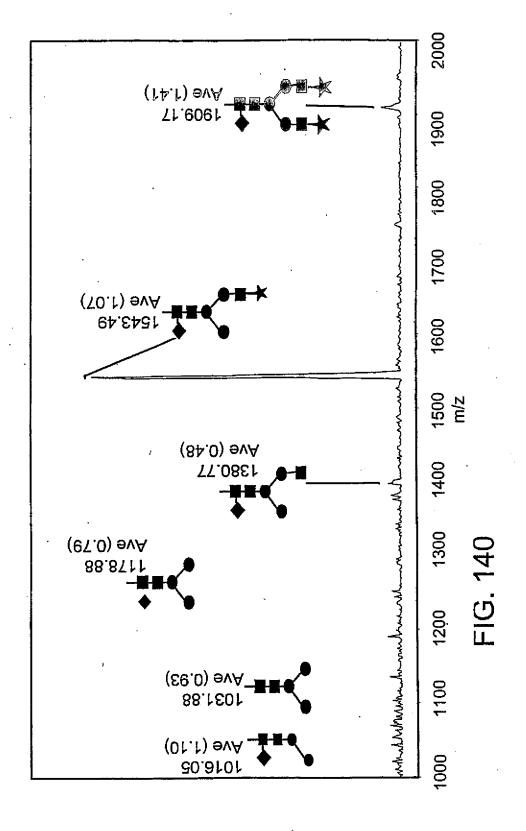
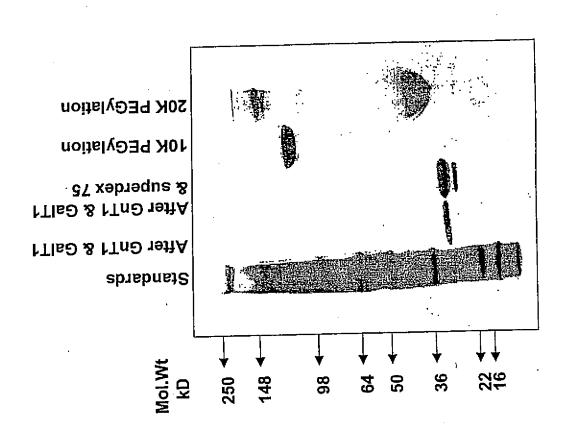


FIG. 138

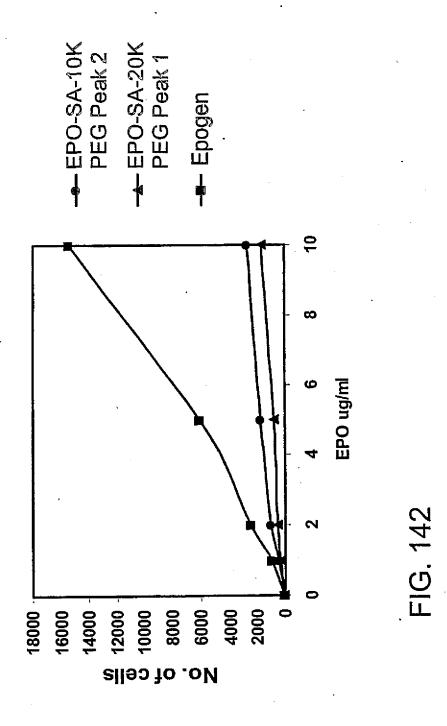








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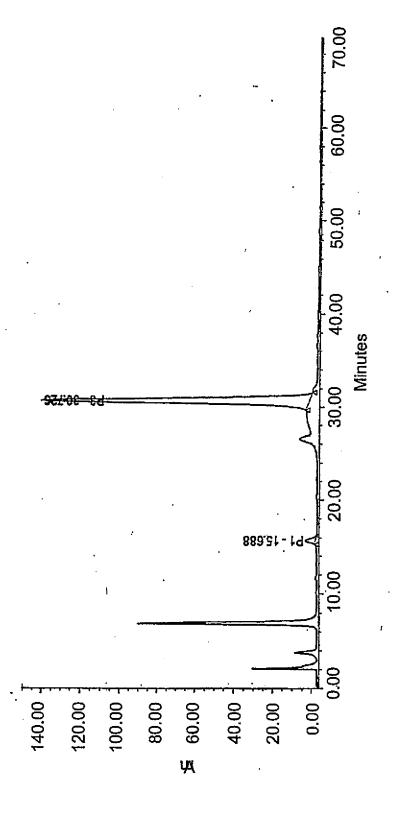
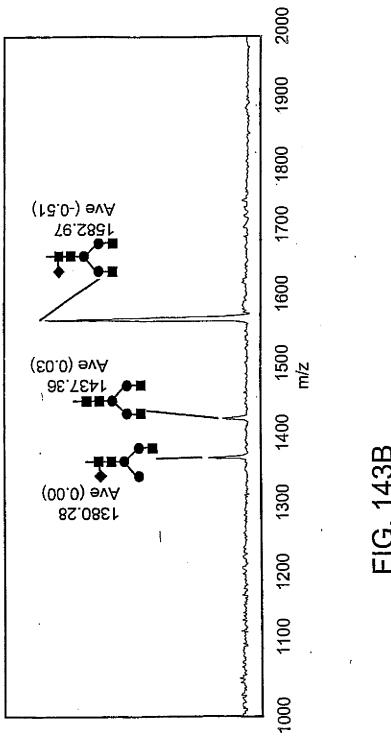
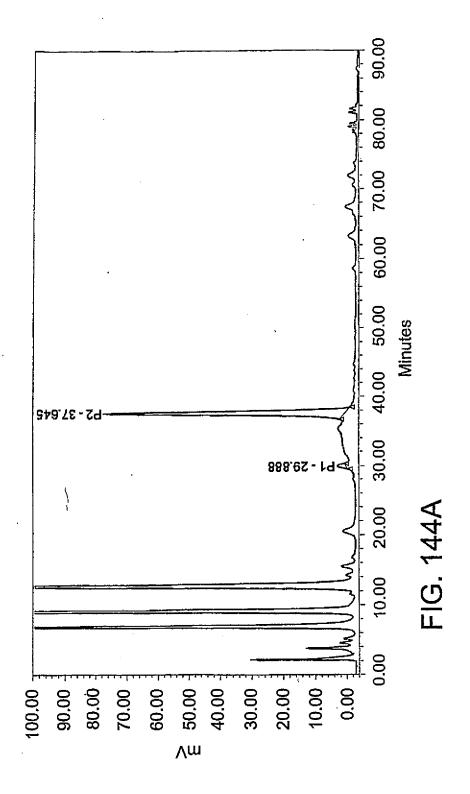
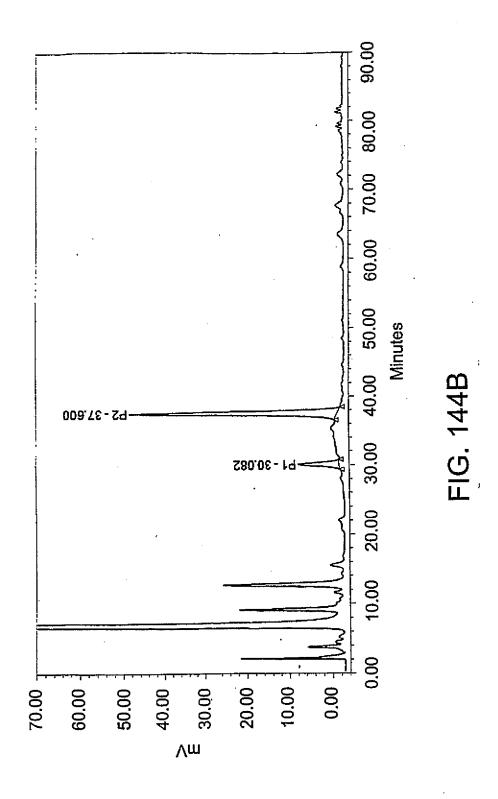
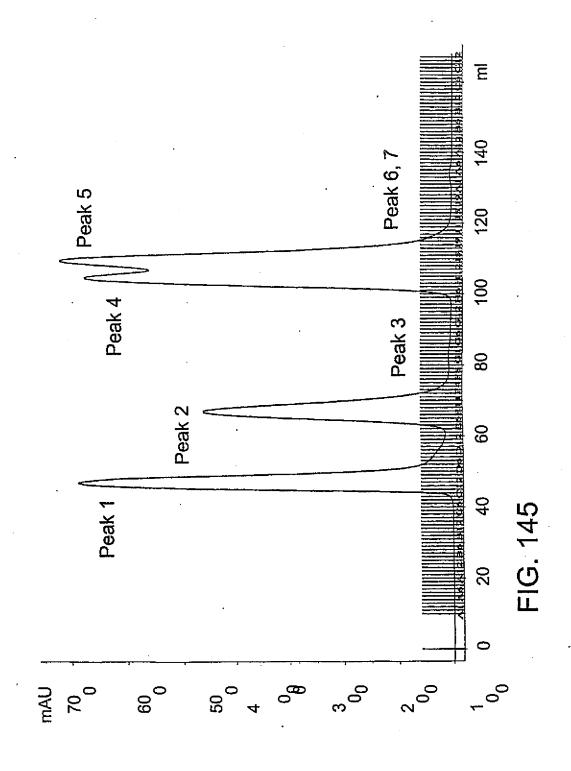


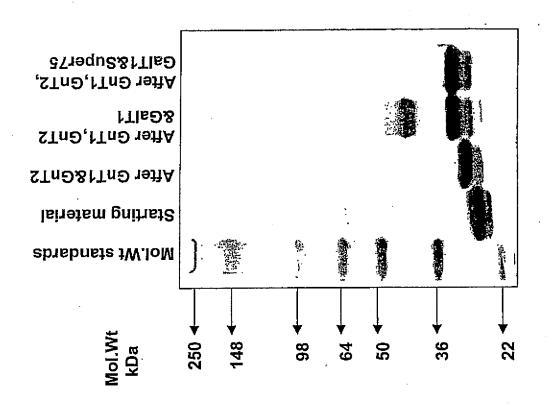
FIG. 143A

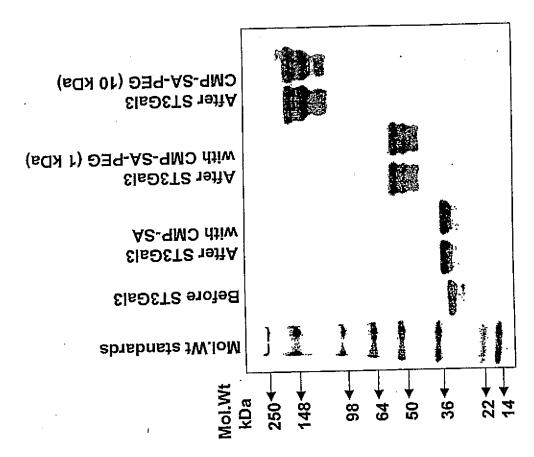




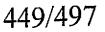


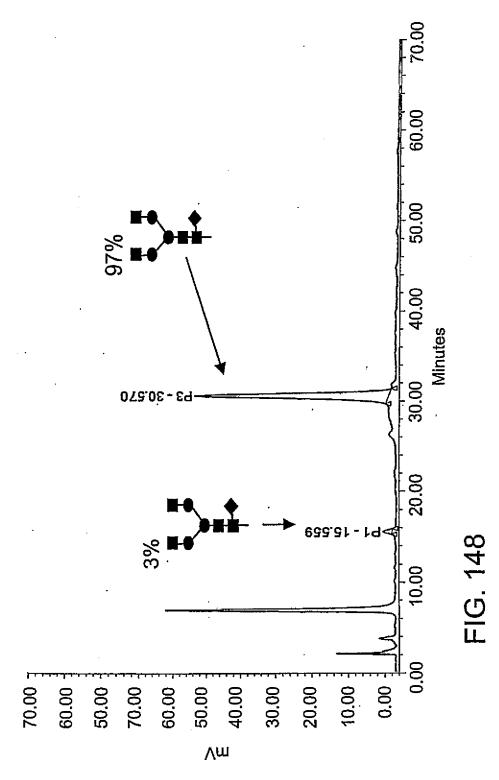


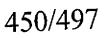


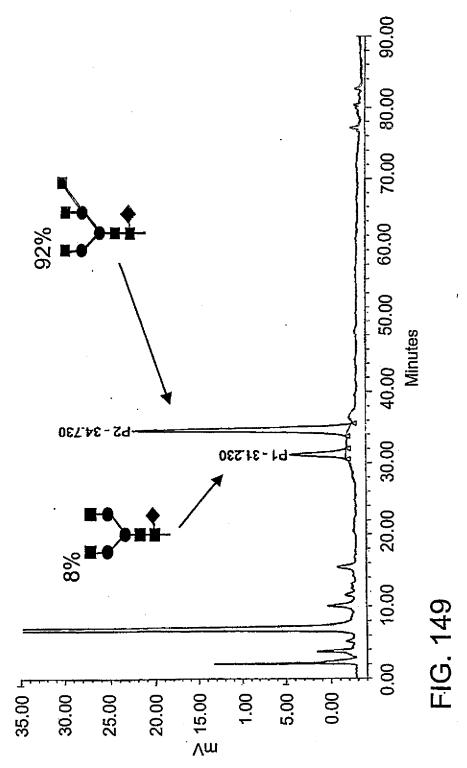


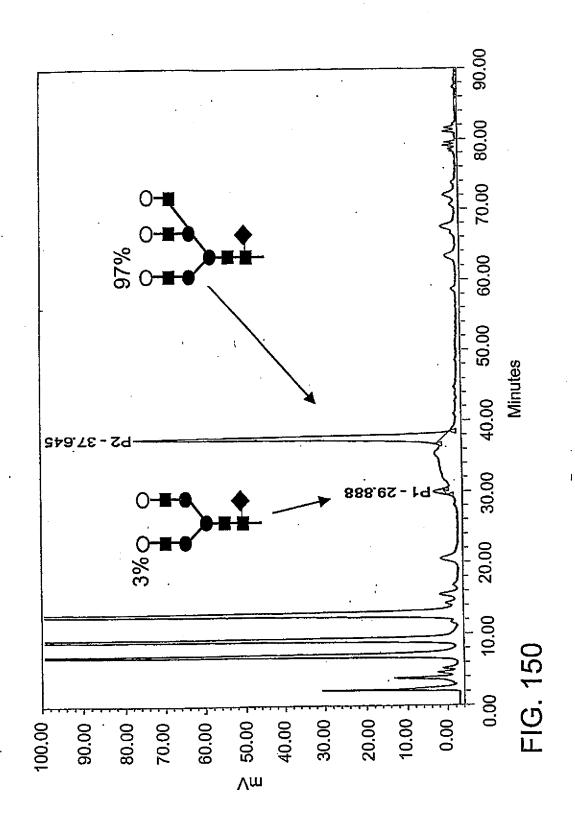
448/497

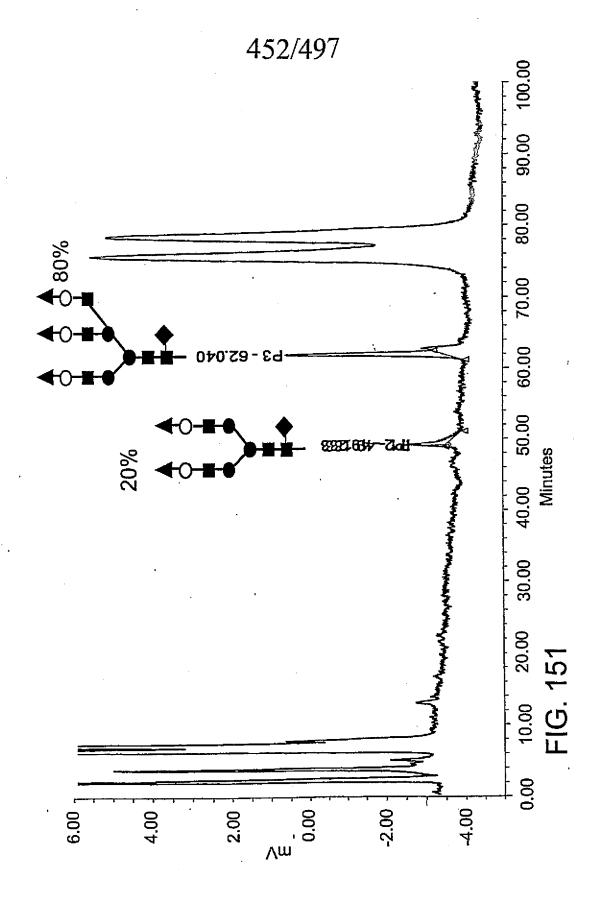


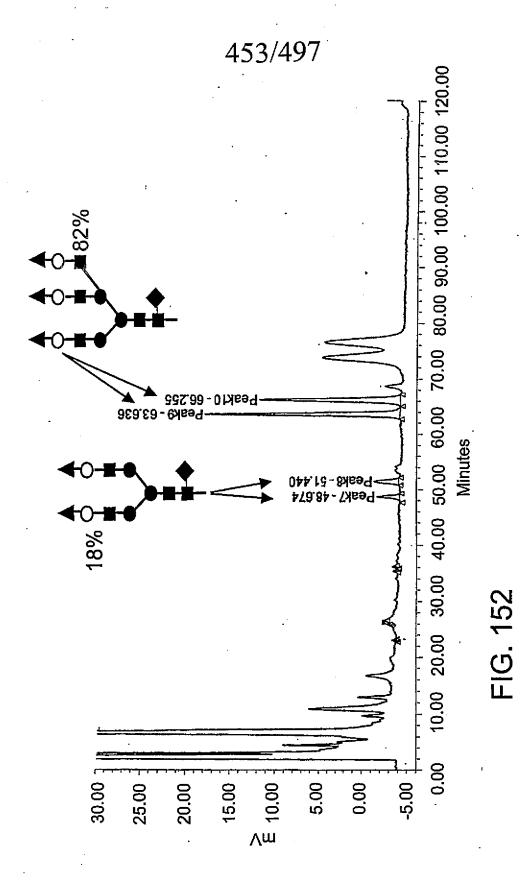


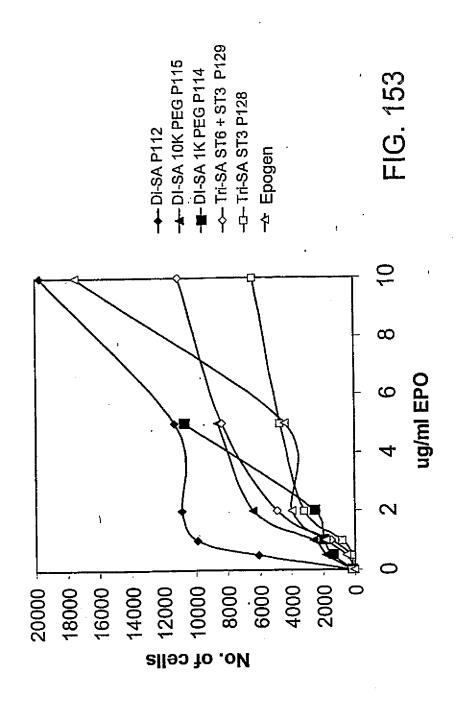












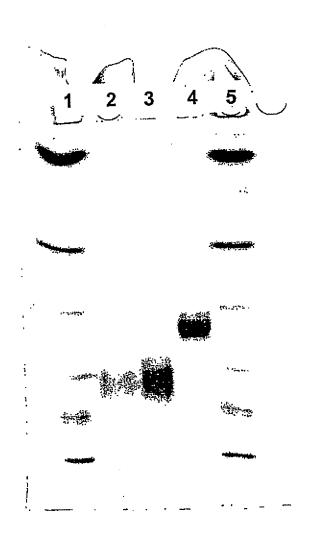


FIG. 154

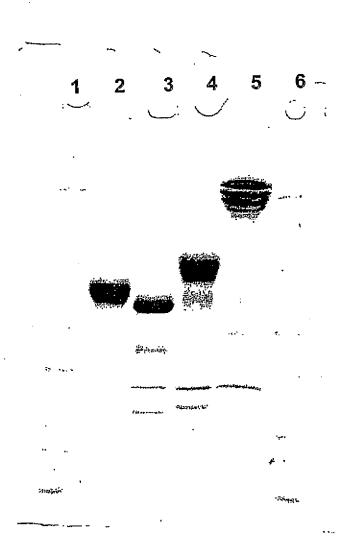
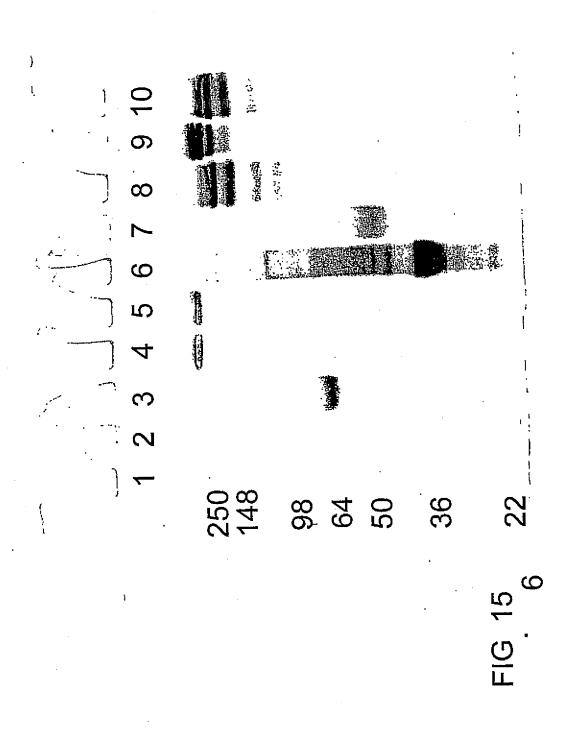


FIG. 155



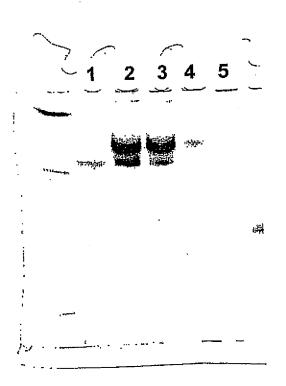
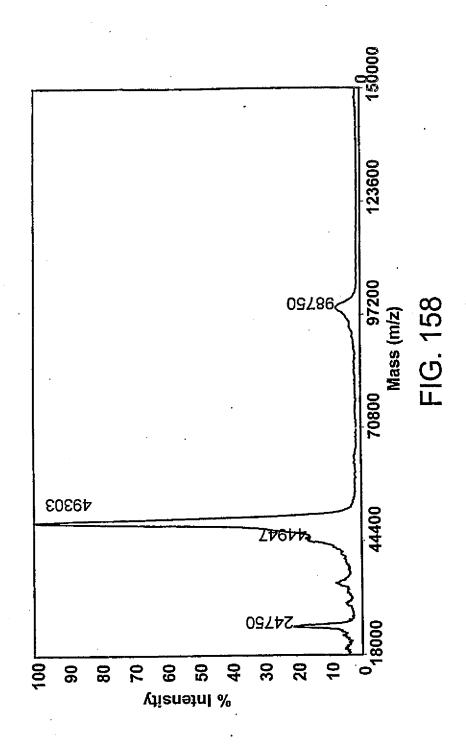
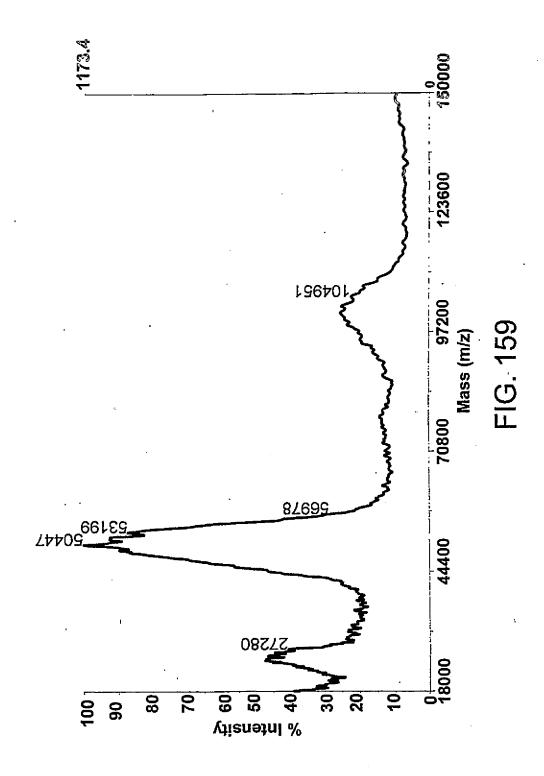
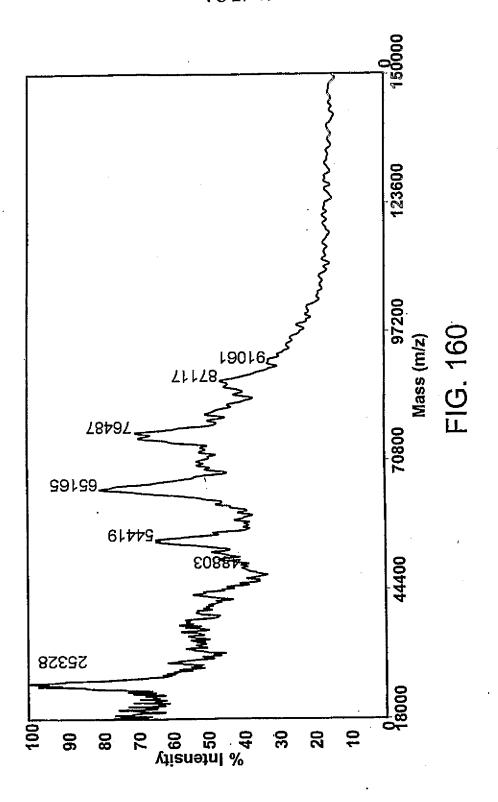


FIG. 157





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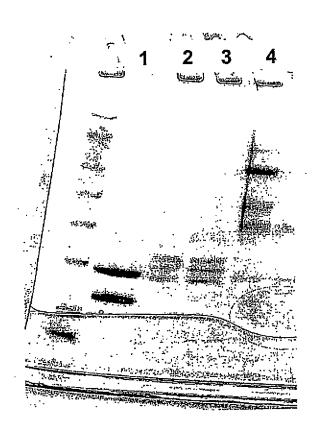


FIG. 161

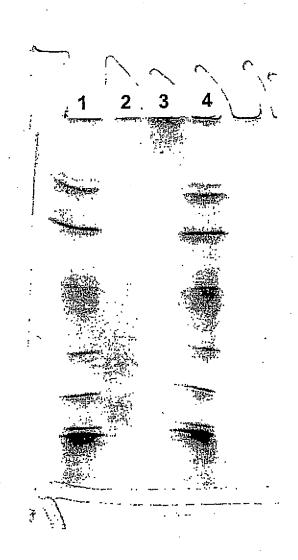


FIG. 162

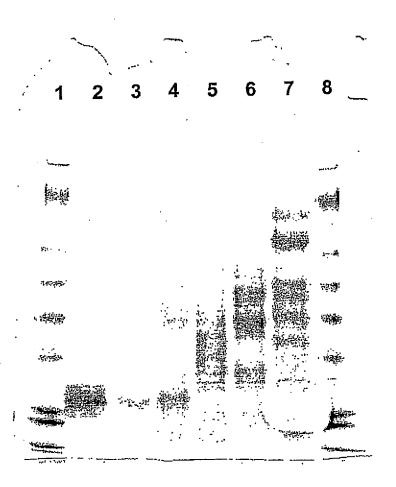


FIG. 163

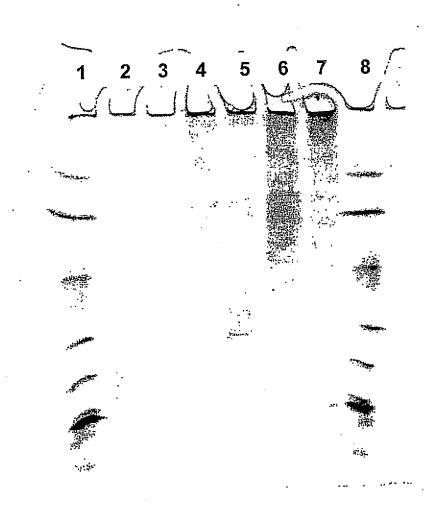


FIG. 164

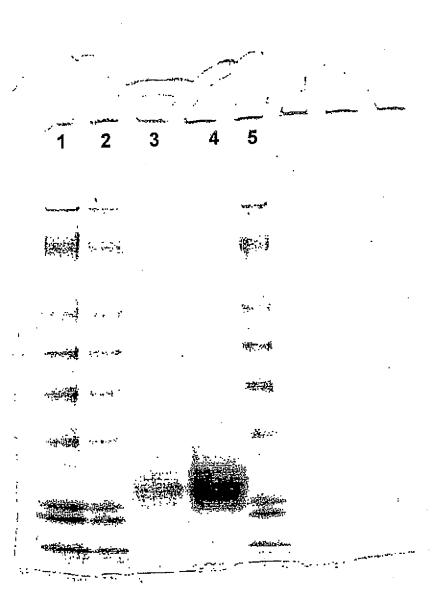


FIG. 165

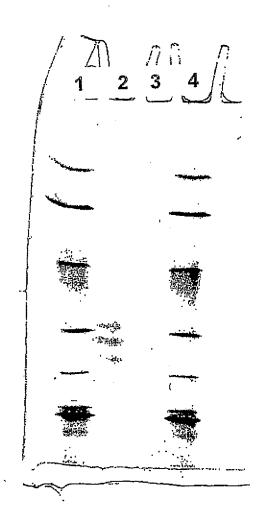


FIG. 166

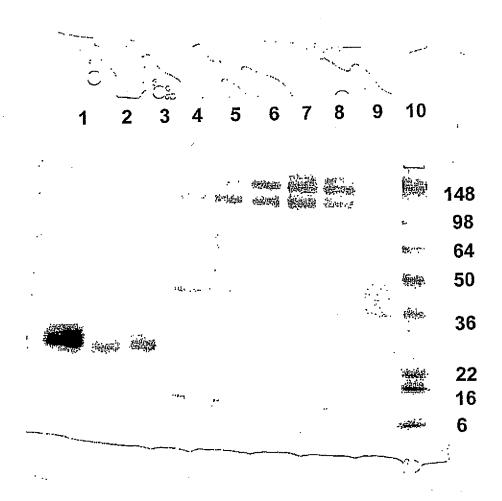


FIG. 167

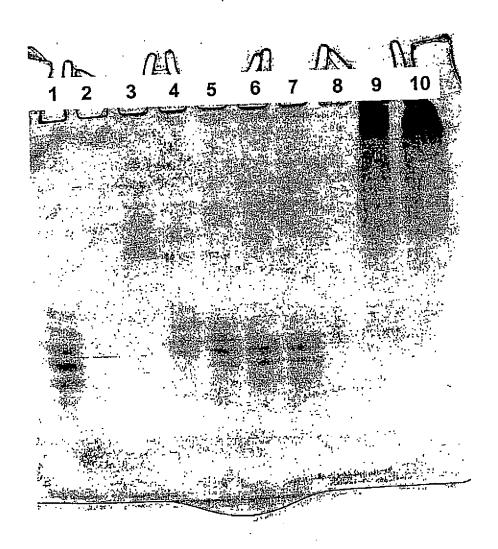
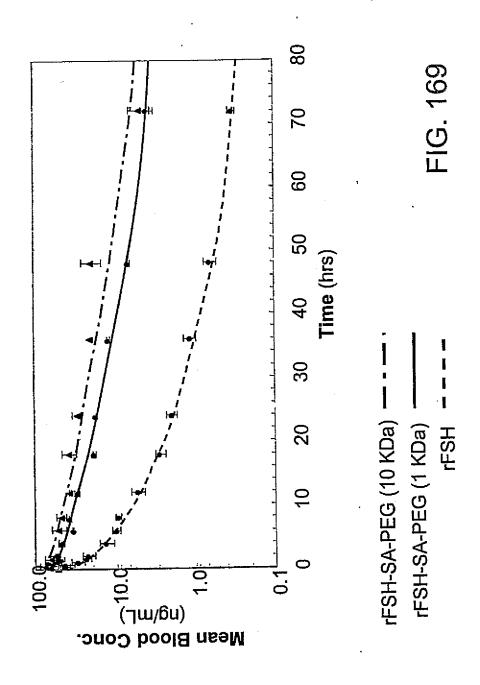
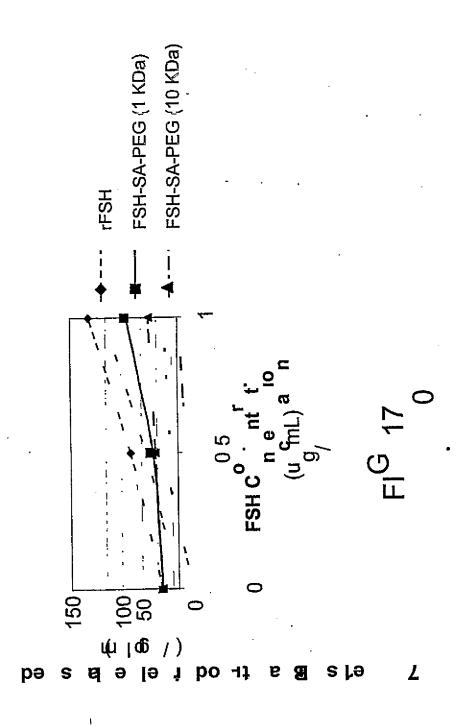
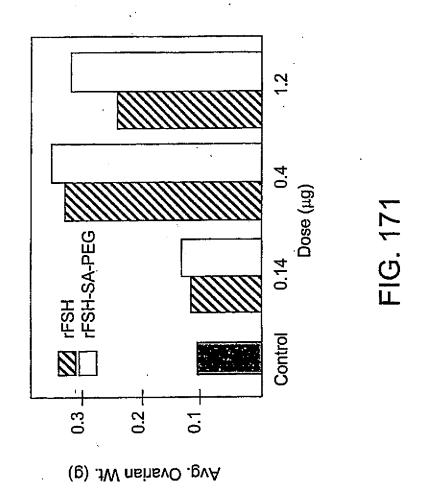
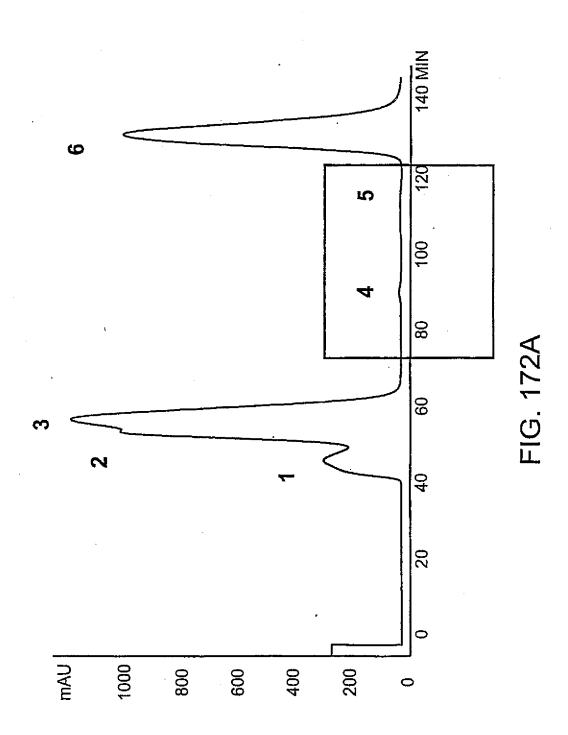


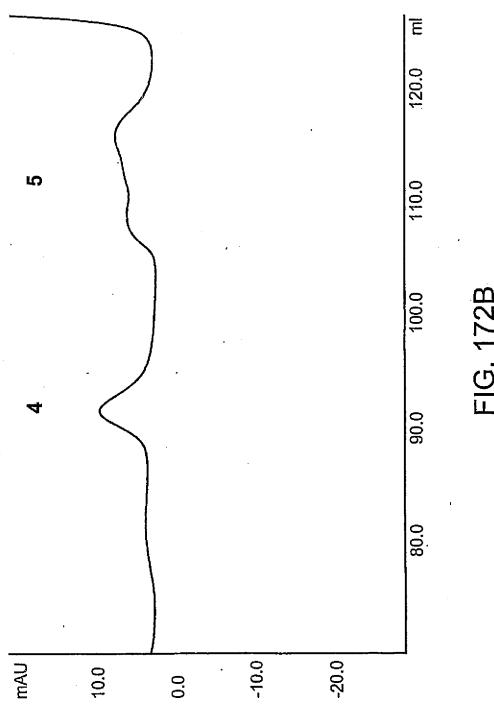
FIG. 168

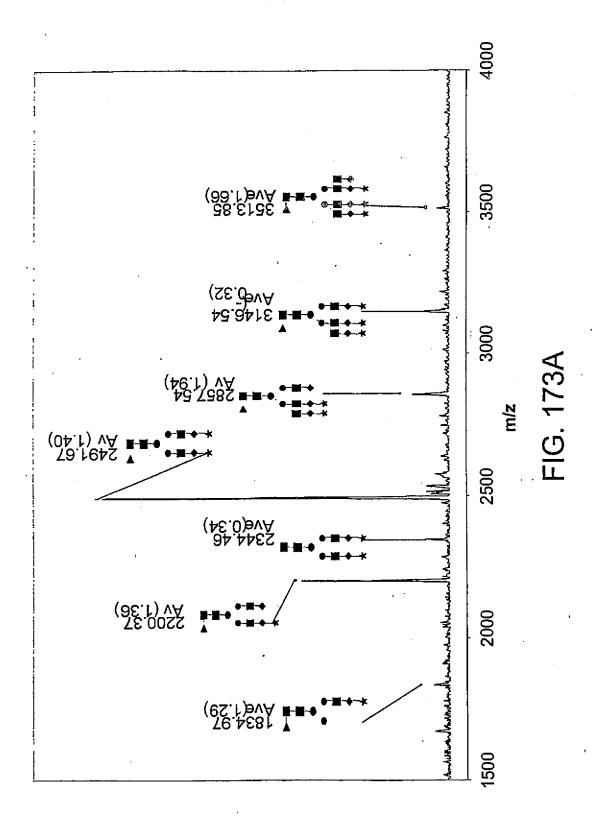


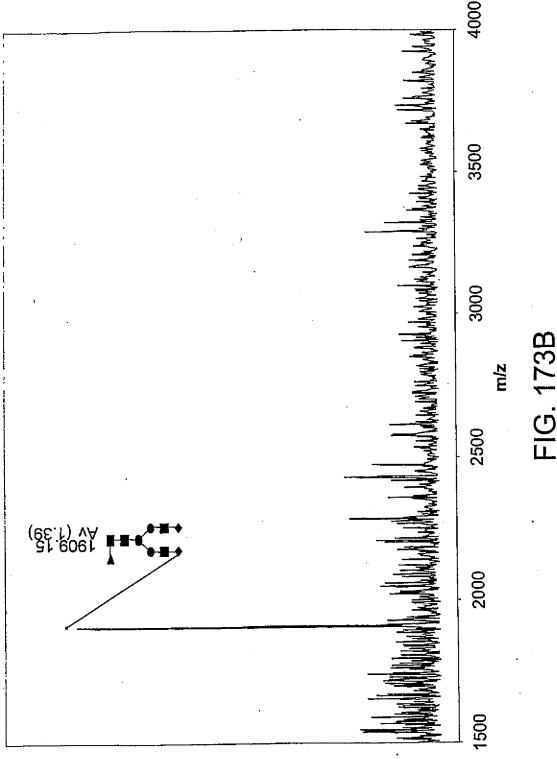












| | 0.1 µg | 0.5 µg | า µg บ.า µg บ.ว µg (fetuin only) | 6 กี เ.บ | 6ri c.u | । मध (fetuin only) | |
|------------------------------------|--------|------------|-------------------------------------|----------|----------|-----------------------|---|
| Fetuin | | | | | | • | ٠ |
| Asialo fetuin | | | | | <i>:</i> | • | |
| purified IFN-β ® | Ø | @ . | | | | | |
| purified IFN-β desialylated peak 4 | | | | ® | | | |
| purified IFN-β desialylated peak 5 | | | | 4. · | 0 | ę | |
| | Z | MAA blot | ¥ | 11 | ECL blog | | |
| | | | | | | | |

FIG. 174

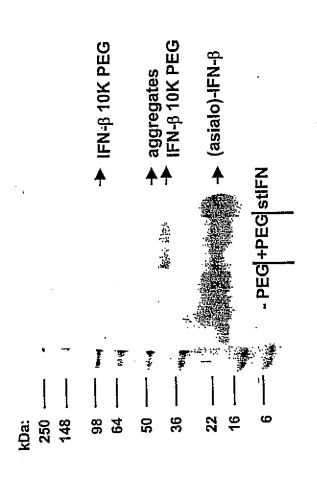
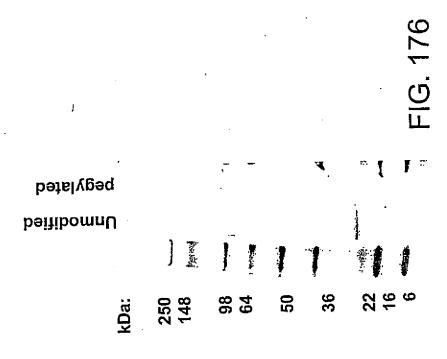
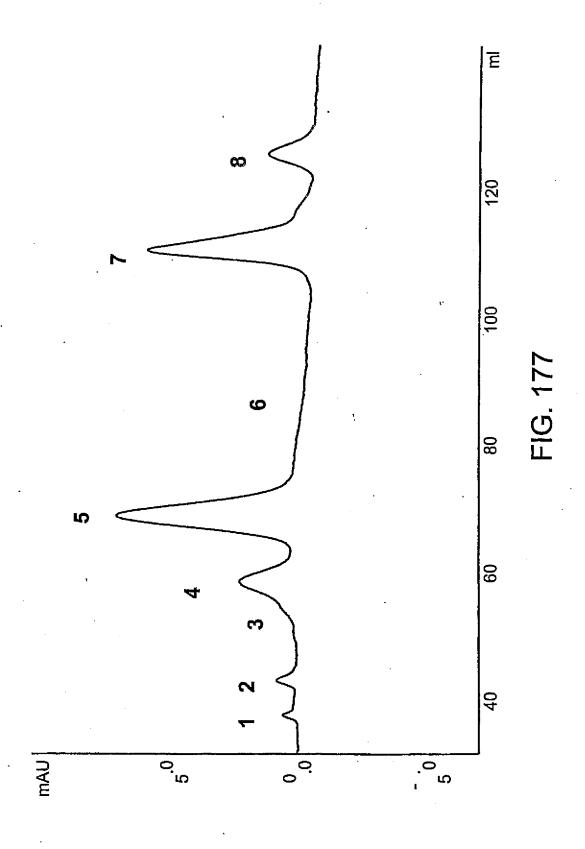
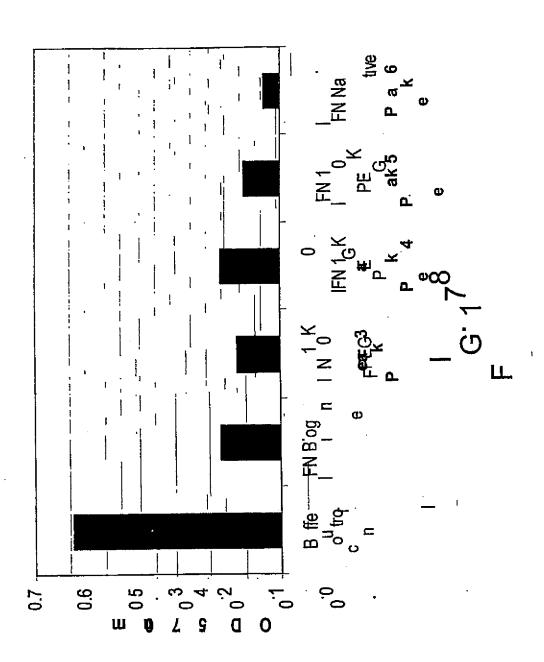


FIG. 175

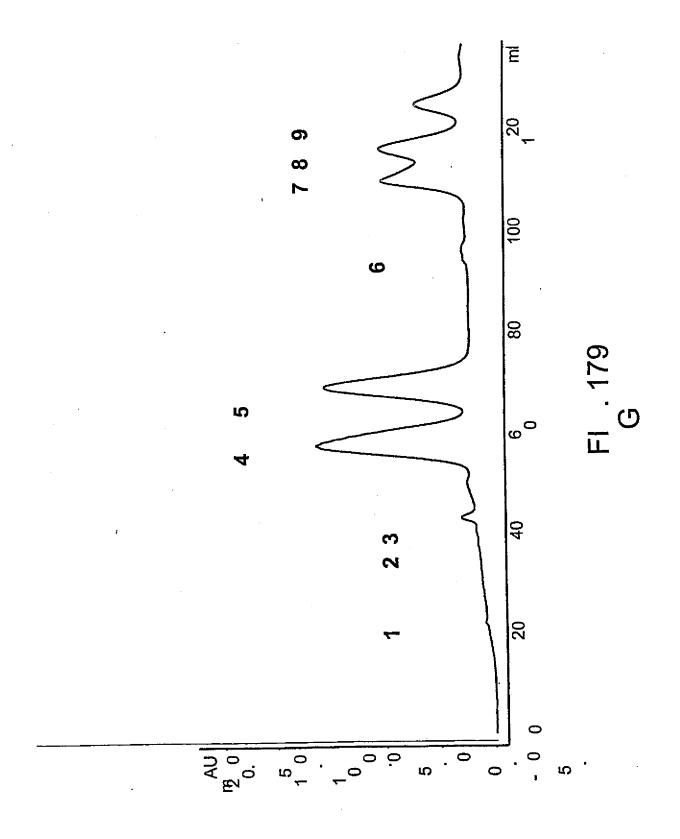


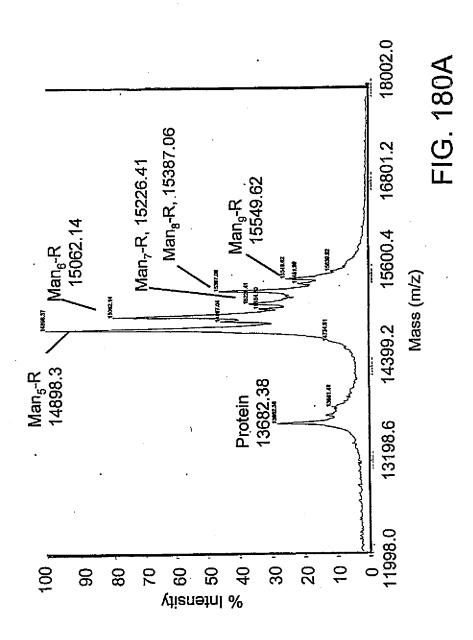


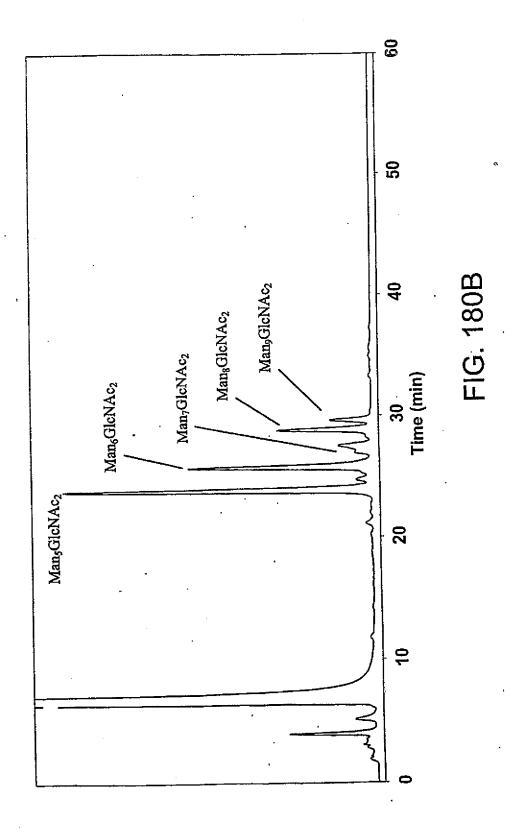
481/497

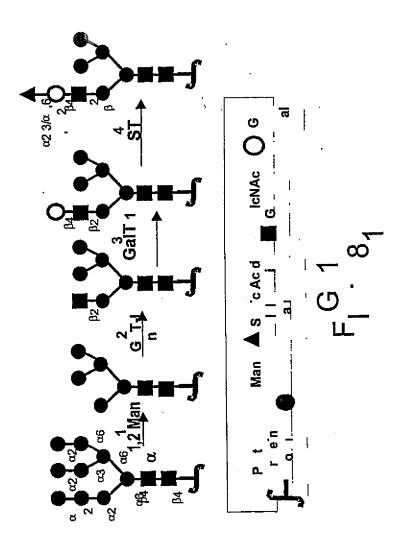


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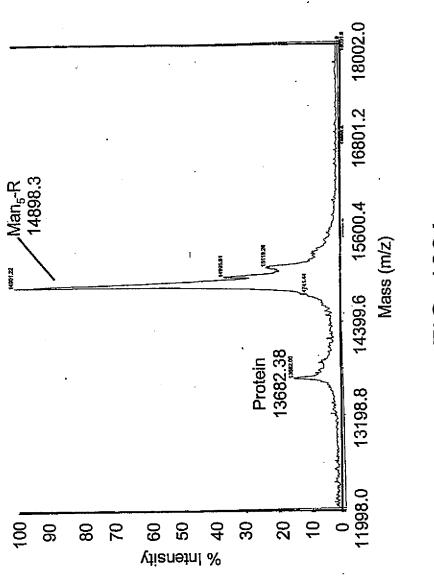
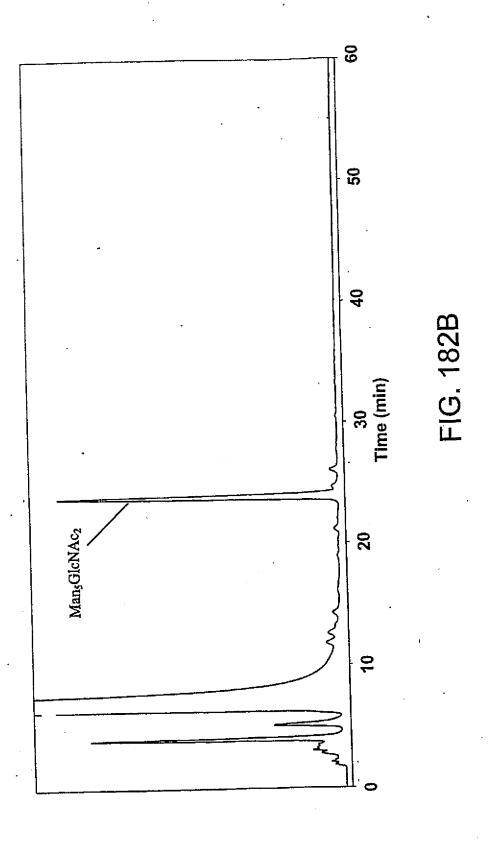
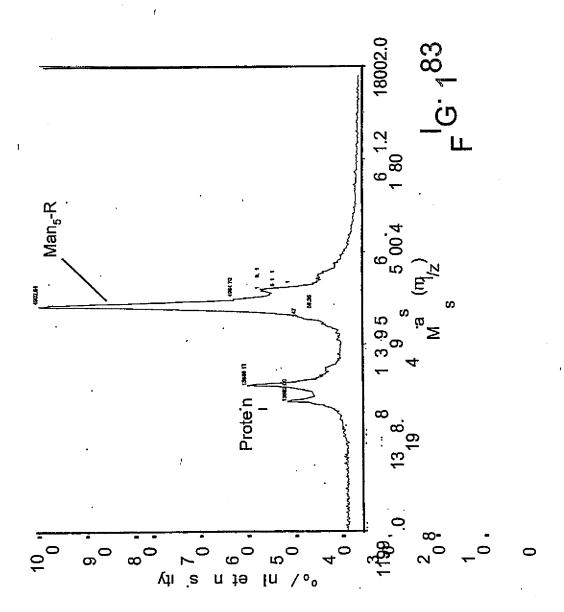
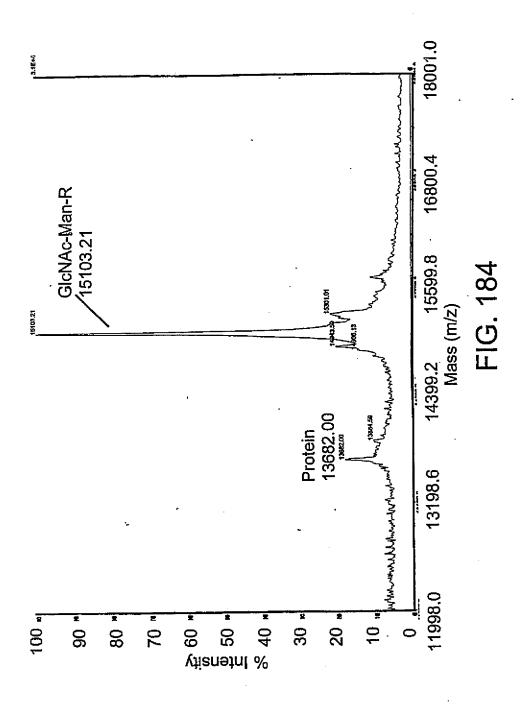


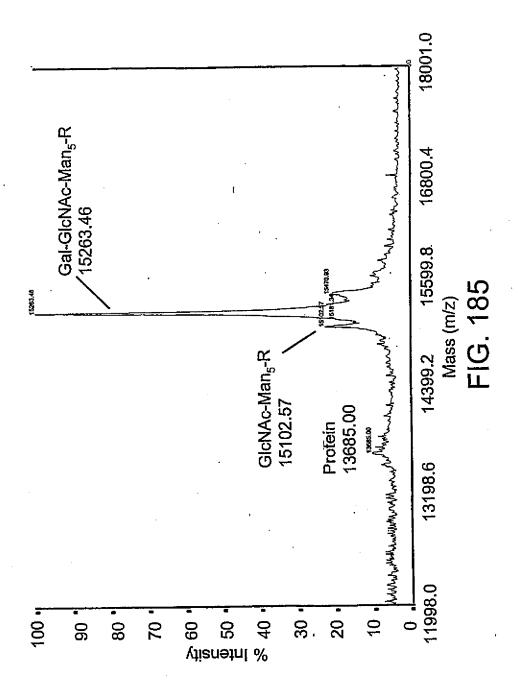
FIG. 182A

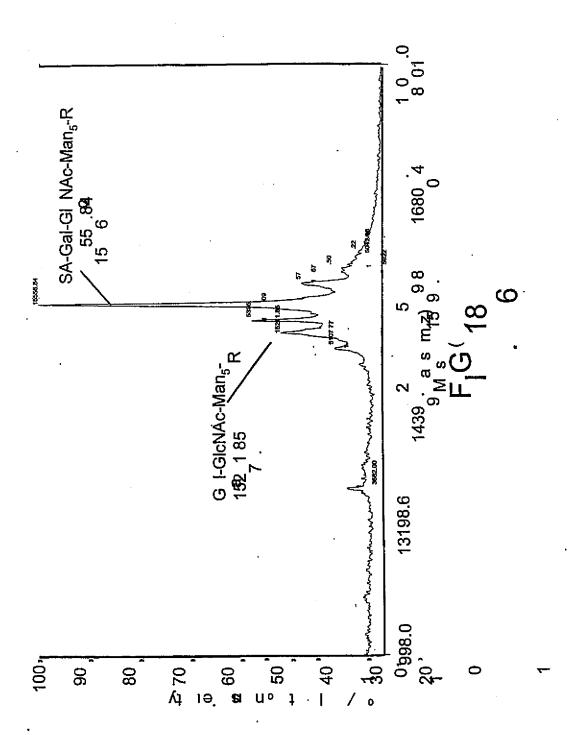
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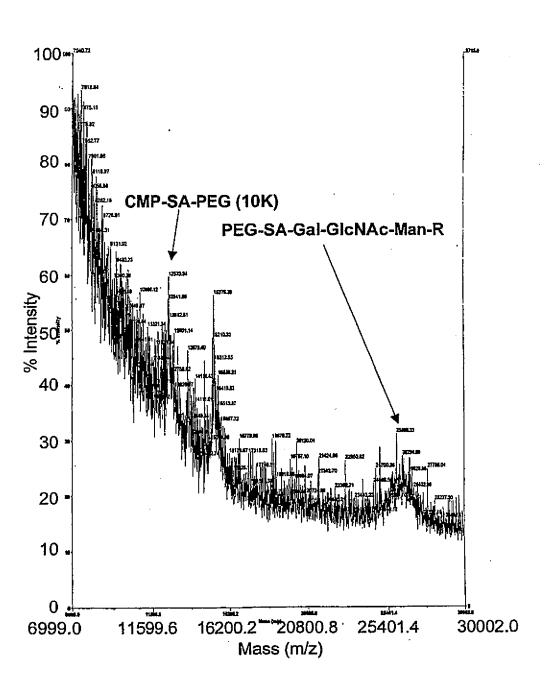


FIG. 187A

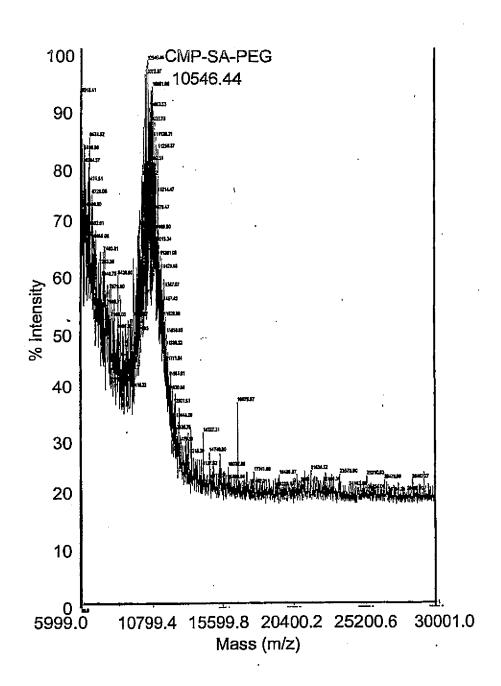
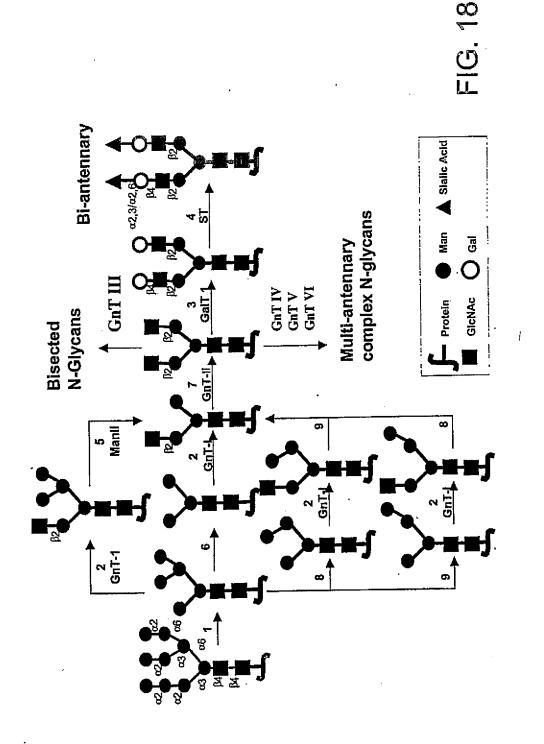
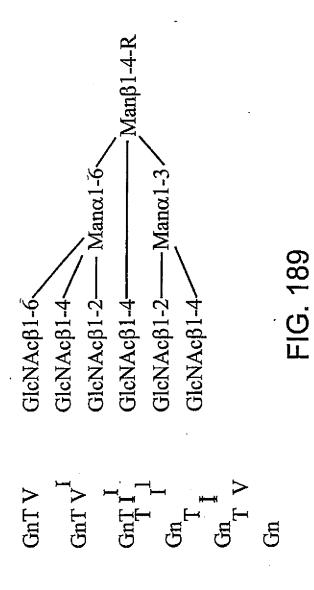


FIG. 187B





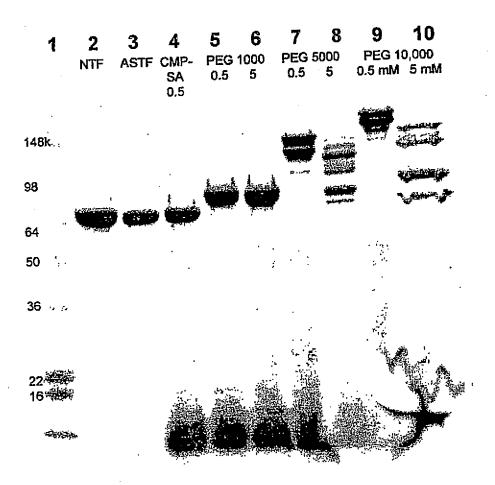


FIG. 190

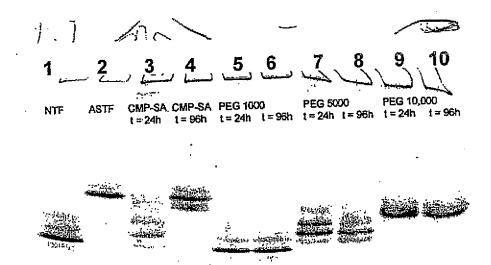


FIG. 191

- <110> Neose Technologies, Inc.
 DeFrees, Shawn
 Zopf, David
 Bayer, Robert
 Hakes, David
 Chen, Xi
 Bowe, Caryne
- <120> GLYCOPEGYLATION METHODS AND PROTEINS/PEPTIDES PRODUCED BY THE METHODS
- <130> 040853-01-5051WO
- <150> US 60/328,523
- <151> 2001-10-10
- <150> US 60/334,233
- <151> 2001-11-28
- <150> US 60/334,301
- <151> 2001-11-28
- <150> US 60/344,692
- <151> 2001-10-19
- <150> US 60/387,292
- <151> 2002-06-07
- <150> US 60/391,777
- <151> 2002-06-25
- <150> US 60/396,594.
- <151> 2002-07-17
- <150> US 60/404,249
- <151> 2002-08-16
- <150> US 60/407,527
- <151> 2002-08-28
- <150> PCT/US02/32263
- <151> 2002-10-09
- <150> US 10/360,779
- <151> 2003-02-19
- <150> US 10/360,770
- <151> 2003-01-06
- <150> US 10/287,994
- <151> 2002-11-05
- <160> 75
- <170> PatentIn version 3.2
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WO 2004/099231

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ggeettttee tetaccaggg getectgeag geeetggaag ggateteece egagttgggt

cccaccttgg acacactgca gctggacgtc gccgactttg ccaccaccat ctggcagcag

atggaagaac tgggaatggc ccctgccctg cagcccaccc agggtgccat gccggccttc

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<210> 2

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<212> PRT .

Homo sapiens <213>

<400> 2

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Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln

Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val

Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys

Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser 70

Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser

Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp 100

Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro 115

Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe

Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe 145 150 .155 160

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taggatatgt aaatagatac acagtgtata tgtgattaaa atataatggg agattcaatc 240

agaaaaaagt ttctaaaaag gctctggggt aaaagaggaa ggaaacaata atgaaaaaaa 300

tgtggtgaga aaaacagctg aaaacccatg taaagagtgt ataaagaaag caaaaagaga 360

agtagaaagt aacacagggg cattiggaaa atgtaaacga gtatgttccc tatttaaggc 420

taggcacaaa gcaaggtctt cagagaacct ggagcctaag gtttaggctc acccatttca 480

accagtetag cagcatetge aacatetaca atggeettga cetttgettt actggtggee 540

ctcctggtgc tcagctgcaa gtcaagctgc tctgtgggct gtgatctgcc tcaaacccac 600

agectgggta geaggaggae ettgatgete etggeacaga tgaggagaat etetettte 660

tcctgcttga aggacagaca tgactttgga tttccccagg aggagtttgg caaccagttc 720

caaaaggctg aaaccatccc tgtcctccat gagatgatcc agcagatctt caatctcttc 780

agcacaaagg actcatctgc tgcttgggat gagaccctcc tagacaaatt ctacactgaa 840

ctctaccagc agctgaatga cctggaagcc tgtgtgatac agggggtggg ggtgacagag 900

actoccotga tgaaggagga ctccattotg gotgtgagga aatacttoca aagaatoact 960

ctctatctga aagagaagaa atacagccct tgtgcctggg aggttgtcag agcagaaatc 1020

atgagatett tttetttgte aacaaaettg caagaaagtt taagaagtaa ggaatgaaaa 1080

ctggttcaac atggaaatga ttttcattga ttcgtatgcc agctcacctt tttatgatct 1140

gccatttcaa agactcatgt ttctgctatg accatgacac gatttaaatc ttttcaaatg 1200

tttttaggag tattaatcaa cattgtattc agctcttaag gcactagtcc cttacagagg 1260

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ctgattacag aataactggt acacttcatt tgtccatcaa tattatattc aagatataag 1560

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Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Arg Ile Ser 35 40 45

Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu 50 55 60

Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His 65 70 75 80

gcttcaagca ttcttcaacc agcagatgct gtttaagtga ctgatggcta atgtactgca

660

PCT/US2004/011494 WO 2004/099231

aatgaaagga cactagaaga ttttgaaatt tttattaaat tatgagttat ttttattat 720

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<211> 187

<212> PRT

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Thr Thr Ala Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg

Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg

Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu 55

Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile

Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser

Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val

Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu 120

Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys 135

Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser 145

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WO 2004/099231 PCT/US2004/011494

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tettacagtg atggggacca gtgtgcctca agtccatgcc agaatggggg ctcctgcaag 300

gaccagetee agtectatat etgettetge etceetgeet tegagggeeg gaactgtgag 360

acgcacaagg atgaccagct gatctgtgtg aacgagaacg gcggctgtga gcagtactgc 420

agtgaccaca cgggcaccaa gcgctcctgt cggtgccacg aggggtactc tctgctggca 480

gacggggtgt cctgcacacc cacagttgaa tatccatgtg gaaaaatacc tattctagaa 540

aaaagaaatg ccagcaaacc ccaaggccga attgtggggg gcaaggtgtg ccccaaaggg 600

gagtgtccat ggcaggtcct gttgttggtg aatggagctc agttgtgtgg ggggaccctg 660

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Leu His Arg Arg Arg Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro 35 40 45

Gly Ser Leu Glu Arg Glu Cys Lys Glu Glu Gln Cys Ser Phe Glu Glu 50 55 60

Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg Thr Lys Leu Phe Trp Ile 65 70 75 80

Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys Gln Asn Gly 85 90 95

Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro 100 105 110

Ala Phe Glu Gly Arg Asn Cys Glu Thr His Lys Asp Asp Gln Leu Ile 115 120 125

Cys Val Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr 130 135 140

Gly Thr Lys Arg Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala 145 150 155 . 160

Asp Gly Val Ser Cys Thr Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile 165 170 175

Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys Pro Gln Gly Arg Ile Val 180 185 190

Gly Gly Lys Val Cys Pro Lys Gly Glu Cys Pro Trp Gln Val Leu Leu 195 200 205

Leu Val Asn Gly Ala Gln Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile 210 215 220

Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg 225 230 235 240

Asn Leu Ile Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly 245 250 255

Asp Glu Gln Ser Arg Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr 260 265 270

Val Pro Gly Thr Thr Asn His Asp Ile Ala Leu Leu Arg Leu His Gln 275 280 285

Pro Val Val Leu Thr Asp His Val Val Pro Leu Cys Leu Pro Glu Arg 290 295 300

Thr Phe Ser Glu Arg Thr Leu Ala Phe Val Arg Phe Ser Leu Val Ser 305 310 315 320

Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu Met 325 330 335

Val Leu Asn Val Pro Arg Leu Met Thr Gln Asp Cys Leu Gln Gln Ser 340 345 350

Arg Lys Val Gly Asp Ser Pro Asn Ile Thr Glu Tyr Met Phe Cys Ala 355 360 365

Gly Tyr Ser Asp Gly Ser Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly 370 375 380

Pro His Ala Thr His Tyr Arg Gly Thr Trp Tyr Leu Thr Gly Ile Val 385 390 395 400

Ser Trp Gly Gln Gly Cys Ala Thr Val Gly His Phe Gly Val Tyr Thr 405 410 415

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Pro Arg Pro Gly Val Leu Leu Arg Ala Pro Phe Pro 435 440

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gagagagaat gtatggaaga aaagtgtagt tttgaagaac cacgagaagt ttttgaaaac 240

actgaaaaga caactgaatt ttggaagcag tatgttgatg gagatcagtg tgagtccaat 300

ccatgtttaa atggcggcag ttgcaaggat gacattaatt cctatgaatg ttggtgtccc 360

tttggatttg aaggaaagaa ctgtgaatta gatgtaacat gtaacattaa gaatggcaga 420

tgcgagcagt tttgtaaaaa tagtgctgat aacaaggtgg tttgctcctg tactgaggga 480

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Homo sapiens <213>

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Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu 25 20

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn

| | | | | | | | | | | • | | | | _ | _ |
|------------|------------|--------------|--------------|--------------|------------|------------|--------------|------------|------------|-------------|------------|------------|----------------------|------------|--------------|
| Ser (| 31y 50 | Lys | Leu | Glu | Glu | Phe 55 | ۷al | Gln | Gly | Asn | Leu 60 | Glu | Arg | Glu | Cys |
| Met (| Glu | Glu | Lys | Cys | Ser 70 | Phe | Glu | Glu | Pro | Arg 75 | Glu | Val | Phe | Glu | Asn 80 |
| Thr | Glu | Lys | Thr | Thr 85 | Glu | Phe | Trp | Lys | Gln 90 | Tyr | Val | qaA | Gly | Asp 95 | Gln |
| Cys | Glu | Ser | Asn 100 | Pro | Cys | Leu | Asn | Gly 105 | Gly | Ser | Cys | Ъуз | Asp 110 | Asp | Ile |
| Asn | Ser | Tyr 115 | Glu | Cys | Trp | Cys | Pro 120 | Phe | Gly | Phe | Glu | Gly 125 | ГÀз | Asn | Cys |
| Glu | Leu 130 | Asp | Val | Thr | Cys | Asn 135 | Ile | Lys | Asn | Gly | Arg 140 | Cys | Glu | Gln | Phe |
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| Tyr | Arg | Leu | Ala | Glu 165 | Asn | Gln | Lys | Ser | Cys 170 | Glu | Pro | Ala | ۷al | Pro 175 | Phe |
| Pro | Cys | Gly | Arg 180 | Val | Ser | Val | Ser | Gln 185 | Thr | Ser | Lys | Leu | Thr 190 | Arg | Ala |
| Glu | Ala | Val 195 | Phe | Pro | Asp | ۷al | Asp 200 | Tyr | Val | Asn | Pro | Thr 205 | Glu | Ala | Glu |
| Thr | Ile 210 | Leu | Asp | Asn | Ile | Thr 215 | Gln | Gly | Thr | Gln | Ser 220 | Phe | Asn | Asp | Phe |
| Thr 225 | Arg | Val | Val | Gly | Gly 230 | Glu | Asp | Ala | Lys | 235 | Gly | Gln | Phe | Pro | Trp 240 |
| Gln | Val | Val | Leu | Asn 245 | Gly | Lys | Val | Asp | Ala 250 | Phe | . Cys | Gly | Gly | Ser 255 | Ile |
| Val | Asn | Glu | . Lys 260 | Trp | Ile | Val | Thr | Ala 265 | Ala | His | ; Суз | : Val | . G lu 270 | Thr | Gly |
| Val | Lуs | Ile 275 | | . Val | . Val | Ala | G1y 280 | Glu | His | a Asr | ı Ile | Glu 285 | ı Glu | ı Thi | Glu |
| His | Thr 290 | | Gln | Lys | : Arg | Asn 295 | val | . Ile | a Arç | g Ala | 300 | : Ile | e Pro | His | His |
| Asn 305 | Tyr | Asr | ı Ala | a Ala | Ile 310 | Asr | ı Lys | . Tyr | Ası | n His 31 | s Asp 5 | o Ile | e Ala | a Lei | 1 Leu 320 |
| Glu | Leu | . Asp | Glu | 1 Pro 325 | | ı Val | L Leu | ı Asr | 330 | r Ty: | r Val | L Thi | r Pro | 33! | ∍ Суз 5 |
| Ile | Ala | Asp | ь Lys 34(| | а Туг | Th: | c Asr | 11e 345 | e Pho | e Le | u Ly: | s Phe | e Gly 35 | y Se: | r Gly |
| Tyr | Val | . Sei 355 | | y Trj | o Alá | a Arg | g Val 360 | L Phe | e Hi | s Ly | s Gl | y Ar | g Se: 5 | r Al | a Leu |

Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu 370 375 380

Arg Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe 385 390 395 400

His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His
405 410 415

Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp 420 425 430

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gagaaccaca cggcgtgcca ctgcagtact tgttattatc acaaatctta aatgttttac 360

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<213> Homo sapiens

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Glu Cys Thr Leu Gln Glu Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro

Ile Leu Gln Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro

Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn Val Thr Ser Glu 70

Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly

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<211> 129

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Glu Glu Cys Arg Phe Cys Ile Ser Ile Asn Thr Thr Trp Cys Ala Gly

Tyr Cys Tyr Thr Arg Asp Leu Val Tyr Lys Asp Pro Ala Arg Pro Lys

Ile Gln Lys Thr Cys Thr Phe Lys Glu Leu Val Tyr Glu Thr Val Arg 65

Val Pro Gly Cys Ala His His Ala Asp Ser Leu Tyr Thr Tyr Pro Val

Ala Thr Gln Cys His Cys Gly Lys Cys Asp Ser Asp Ser Thr Asp Cys 110

Thr Val Arg Gly Leu Gly Pro Ser Tyr Cys Ser Phe Gly Glu Met Lys 125 120 115

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15 <400>

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gaggtacctc ttggaggcca aggaggccga gaatatcacg acgggctgtg ctgaacactg .360

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193 <211>

<212> PRT

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<400> 16

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Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu

Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu 35

Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu

Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg 70

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Met Giu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu 90 85

Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser

Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly 120

Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Arg Ala Gln Lys Glu 135 130

Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile 1.50

Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu 170

Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp 185 180

Arg

<210> 17

<211> 435

<212> DNA

Homo sapiens <213>

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egteteetga acetgagtag agacactget getgagatga atgaaacagt agaagteate

tcagaaatgt ttgacctcca ggagccgacc tgcctacaga cccgcctgga gctgtacaag 240

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<213> Homo sapiens

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Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp 40 35

Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe

Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys

Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met

Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser

Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys 115

Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu 140 135 130

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<211> 501

<212> DNA

<213> Homo sapiens

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gaggagagtg acagaaaaat aatgcagagc caaattgtct ccttttactt caaacttttt 240

aaaaacttta aagatgacca gagcatccaa aagagtgtgg agaccatcaa ggaagacatg 300

aatgtcaagt tittcaatag caacaaaaag aaacgagatg acttcgaaaa gctgactaat

tattoggtaa ctgacttgaa tgtccaacgc aaagcaatac atgaactcat ccaagtgatg 420

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<212> PRT

<213> Homo sapiens

<400> 20

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Gly Ser Leu Gly Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu

Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn

Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp

Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe

Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile

Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg 110 100

Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val 120

Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser

Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg 155 150 145

Gly Arg Arg Ala Ser Gln 165

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1352 <211>

<212> DNA

Homo sapiens <213>

<400> 21

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gacagataca teccaecatg atcaggatea eccaacette aacaagatea eccecaacet

ggctgagttc gccttcagcc tataccgcca gctggcacac cagtccaaca gcaccaatat 240

cttcttctcc ccagtgagca tcgctacagc ctttgcaatg ctctccctgg ggaccaaggc 300

tgacactcac gatgaaatcc tggagggcct gaatttcaac ctcacggaga ttccggaggc 360

PCT/US2004/011494 WO 2004/099231

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cgaagaggcc aagaaacaga tcaacgatta cgtggagaag ggtactcaag ggaaaattgt 600

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22 <210>

418 <211>

PRT <212>

<213> Homo sapiens

<400> 22

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Cys Leu Val Pro Val Ser Leu Ala Glu Asp Pro Gln Gly Asp Ala Ala

| Gln L | | Thr 35 | Asp | Thr | Ser | His | His 40 | Asp | Gln | Asp | His | Pro 45 | Thr | Phe | Asn |
|--------------|------------|------------|------------|------------|------------|------------|------------|--------------|--------------|------------|------------|------------|------------|------------|--------------|
| Lys I 5 | le 50 | Thr | Pro | Asn | Leu | Ala 55 | Glu | Phe | Ala | Phe | Ser 60 | Leu | Tyr | Arg | Gln |
| Leu A 65 | Ala | His | Gln | Ser | Asn 70 | Ser | Thr | Asn | Ile | Phe 75 | Phe | Ser | Pro | Val | Ser 80 |
| Ile A | Ala | Thr | Ala | Phe 85 | Ala | Met | Leu | Ser | Leu 90 | Gly | Thr | Lys | Ala | Asp 95 | Thr |
| His A | qs/ | Glu | Ile 100 | Leu | Glu | Gly | Leu | Asn 105 | Phe | Asn | Leu | Thr | Glu 110 | Ile | Pro |
| Glu A | Ala | Gln 115 | Ile | His | Glu | Gly | Phe 120 | Gln | Glu | Leu | Leu | Arg 125 | Thr | Leu | Asn |
| Gln F | Pro 130 | qaA | Ser | Gln | Leu | Gln 135 | Leu | Thr | Thr | Gly | Asn 140 | Gly | Leu | Phe | Leu |
| Ser (| Glu | Gly | Leu | Lys | Leu 150 | Val | Asp | Lys | Phe | Leu 155 | Glu | Asp | Val | Lys | Lys 160 |
| Leu 1 | Tyr | His | Ser | Glu 165 | Ala | Phe | Thr | Val | Asn 170 | Phe | Gly | Asp | Thr | Glu 175 | Glu |
| Ala I | Lys | Lys | Gln 180 | Ile | Asn | Asp | Tyr | Val 185 | Glu | Lys | Gly | Thr | Gln 190 | Gly | Lys |
| Ile V | Val | Asp 195 | Leu | -Val | Lys | Glu | Leu 200 | Asp | Arg | Asp | Thr | Val 205 | Phe | Ala | Leu |
| Val : | Asn 210 | Tyr | Ile | Phe | Phe | Lys 215 | Gly | ГÀз | Trp | Glu | Arg 220 | Pro | Phe | Glu | Val |
| Lys 2 225 | - | | | | 230 | | | | | 235 | | | | | 240 |
| Lys ' | Val | Pro | Met | Met 245 | Lys | Arg | Leu | Gly | Met 250 | Phe | Asn | Ile | Gln | His 255 | Cys |
| Lys : | Lys | Leu | Ser 260 | Ser | Trp | Val | Leu | Leu 265 | Met | Lys | Tyr | Leu | Gly 270 | Asn | Ala |
| Thr . | Ala | Ile 275 | | Phe | Leu | Pro | Asp 280 | Glu | Gly | Lys | Leu | Gln 285 | His | : Leu | Glu |
| Asn | Glu 290 | | Thr | His | Asp | 11e 295 | | Thr | Lys | Phe | Leu 300 | Glu | Asn | ı Glu | ı Asp |
| Arg . 305 | Arg | Ser | Ala | Ser | Leu 310 | | Lev | Pro | Lys | Leu 315 | Ser | Ile | Thr | : Gl | 7 Thr 320 |
| Tyr | Asp | Leu | Lуs | Ser 325 | | Leu | ı Gly | Glr. | 1 Let 330 | ı Gly | ' Ile | . Thr | Lys | 335 | . Phe |
| Ser | Asn | Gly | Ala 340 | | Leu | Ser | Gly | 7 Val 345 | Thr | Glu | Glu | ı Ala | 350 |) Lei | ı Lys |

Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly 355 360 365

Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile 370 380

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Gly Tyr Ser Ser Val Val Cys Val Cys Asn Ala Thr Tyr Cys Asp Ser

Phe Asp Pro Pro Thr Phe Pro Ala Leu Gly Thr Phe Ser Arg Tyr Glu 65 70 75 80

Ser Thr Arg Ser Gly Arg Arg Met Glu Leu Ser Met Gly Pro Ile Gln 85 90 95

Ala Asn His Thr Gly Thr Gly Leu Leu Leu Thr Leu Gln Pro Glu Gln
100 105 110

Lys Phe Gln Lys Val Lys Gly Phe Gly Gly Ala Met Thr Asp Ala Ala 115 120 125

Ala Leu Asn Ile Leu Ala Leu Ser Pro Pro Ala Gln Asn Leu Leu Leu 130 135 140

Lys Ser Tyr Phe Ser Glu Glu Gly Ile Gly Tyr Asn Ile Ile Arg Val 145 150 155 160

Pro Met Ala Ser Cys Asp Phe Ser Ile Arg Thr Tyr Thr Tyr Ala Asp 165 170 175

Thr Pro Asp Asp Phe Gln Leu His Asn Phe Ser Leu Pro Glu Glu Asp 180 185 190

Thr Lys Leu Lys Ile Pro Leu Ile His Arg Ala Leu Gln Leu Ala Gln
195 200 205

Arg Pro Val Ser Leu Leu Ala Ser Pro Trp Thr Ser Pro Thr Trp Leu 210 215 220

Lys Thr Asn Gly Ala Val Asn Gly Lys Gly Ser Leu Lys Gly Gln Pro 225 230 235

Gly Asp Ile Tyr His Gln Thr Trp Ala Arg Tyr Phe Val Lys Phe Leu 245 250 255

Asp Ala Tyr Ala Glu His Lys Leu Gln Phe Trp Ala Val Thr Ala Glu 260 265 270

Asn Glu Pro Ser Ala Gly Leu Leu Ser Gly Tyr Pro Phe Gln Cys Leu

WO 2004/099231 275 280 285

Gly Phe Thr Pro Glu His Gln Arg Asp Phe Ile Ala Arg Asp Leu Gly 290 295 300

PCT/US2004/011494

Pro Thr Leu Ala Asn Ser Thr His His Asn Val Arg Leu Leu Met Leu 305 310 315

Asp Asp Gln Arg Leu Leu Leu Pro His Trp Ala Lys Val Val Leu Thr 325 330 335

Asp Pro Glu Ala Ala Lys Tyr Val His Gly Ile Ala Val His Trp Tyr 340 345 350

Leu Asp Phe Leu Ala Pro Ala Lys Ala Thr Leu Gly Glu Thr His Arg 355 360 365

Leu Phe Pro Asn Thr Met Leu Phe Ala Ser Glu Ala Cys Val Gly Ser 370 380

Lys Phe Trp Glu Gln Ser Val Arg Leu Gly Ser Trp Asp Arg Gly Met 385 390 395 400

Gln Tyr Ser His Ser Ile Ile Thr Asn Leu Leu Tyr His Val Val Gly 405 410 415

Trp Thr Asp Trp Asn Leu Ala Leu Asn Pro Glu Gly Gly Pro Asn Trp 420 425 430

Val Arg Asn Phe Val Asp Ser Pro Ile Ile Val Asp Ile Thr Lys Asp 435 440 445

Thr Phe Tyr Lys Gln Pro Met Phe Tyr His Leu Gly His Phe Ser Lys 450 455

Phe Ile Pro Glu Gly Ser Gln Arg Val Gly Leu Val Ala Ser Gln Lys 465 470 475 480

Asn Asp Leu Asp Ala Val Ala Leu Met His Pro Asp Gly Ser Ala Val 485 490 495

Val Val Val Leu Asn Arg Ser Ser Lys Asp Val Pro Leu Thr Ile Lys
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gtgcctgtca aaagttgcag cgagccaagg tgtttcaacg ggggcacctg ccagcaggcc 300

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Ile Tyr Gln Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn

Arg Val Glu Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser 70

Val Pro Val Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr

Cys Gln Gln Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu

Gly Phe Ala Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr 115

Glu Asp Gln Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser 130

Gly Ala Glu Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro 155 150

Tyr Ser Gly Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His 170 165

Asn Tyr Cys Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val

| Phe | Lys | Ala 195 | Gly | Lys | Tyr | Ser | Ser 200 | Glu | Phe | Cys | | Thr 205 | Pro | Ala | Cys |
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| Ser | Glu 210 | Gly | Asn | Ser | Asp | Cys 215 | Tyr | Phe | Gly | Asn | Gly 220 | Ser | Ala | Tyr | Arg |
| Gly 225 | Thr | His | Ser | Leu | Thr 230 | Glu | Sex | Gly | Ala | Ser 235 | Суз | Leu | Pro | Trp | Asn 240 |
| Ser | Met | Ile | Leu | Ile 245 | Gly | Lys | Val | Tyr | Thr 250 | Ala | Gln | Asn | Pro | Ser 255 | Ala |
| Gln | Ala | Leu | Gly 260 | Leu | Gly | Lys | His | Asn 265 | Tyr | Cys | Arg | Asn | Pro 270 | Asp | Gly |
| Asp | Ala | Lys 275 | Pro | Trp | Cys | His | Val 280 | Leu | Lys | Asn | Arg | Arg 285 | Leu | Thr | Trp |
| Glu | Tyr 290 | Cys | Asp | Val | Pro | Ser 295 | Суз | Ser | Thr | Сув | Gly 300 | Leu | Arg | Gln | Tyr |
| Ser 305 | Gln | Pro | Gln | | Arg 310 | Ile | Lys | Gly | Gly | Leu 315 | Phe | Ala | Asp | Ile | Ala 320 |
| Ser | His | Pro | Trp | Gln 325 | Ala | Ala | Ile | Phe | Ala 330 | Lys | His | Arg | Arg | Ser 335 | Pro |
| Gly | Glu | Arg | Phe 340 | Leu | Cys | Gly | Gly | Ile 345 | Leu | Ile | Ser | Ser | Cys 350 | Trp | Ile |
| Leu | Ser | Ala 355 | Ala | His | Cys | Phe | Gln 360 | Glu | Arg | Phe | Pro | Pro 365 | His | His | Leu |
| Thr | Val 370 | Ile | Leu | Gly | Arg | Thr 375 | | Arg | Val | Val | Pro 380 | Gly | Glu | Glu | Glu |
| Gln 385 | | Phe | Glu | Val | Glu 390 | Lys | Tyr | Ile | Val | His 395 | Lys | Glu | Phe | Asp | Asp 400 |
| Asp | Thr | Tyr | Asp | Asn 405 | Asp | Ile | Ala | Leu | Leu 410 | Gln | Leu | Lys | Ser | Asp 415 | Ser |
| Ser | Arg | Cys | Ala 420 | | Glu | Ser | Ser | Val 425 | Val | Arg | Thr | Val | Cys 430 | Leu | Pro |
| Pro | Ala | Asp 435 | | Gln | Leu | . Pro | Asp 440 | Trp | Thr | Glu | Cys | Glu 445 | Lev | . Ser | Gly |
| Tyr | Gly 450 | | His | Glu | Ala | Leu 455 | | Pro | Phe | туг | Sex 460 | Glu | Arg | , Ler | Lys |
| Glu 465 | | His | Val | Arg | Leu 470 | | Pro | Ser | Ser | Arg 475 | Cys | Thr | : Ser | Glr | His 480 |
| Leu | Leu | . Asn | Arg | Thr 485 | | Thr | : Asp | Asn | Met 490 | | . Cys | : Ala | a Gly | / Asp 495 | Thr |
| Arg | Ser | Gl _y | Gly 500 | | Gln | Ala | Asn | Lev 505 | | asp | Ala | Cys | 51r 510 | ı Gly | Asp |

Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val

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<213> Homo sapiens

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156 <211>

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Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr 55

Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys Gln Leu Gln

Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala

Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile 100

Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys

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Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile
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Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser

His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser

Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp 130 135 140

Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu 145 150 155 160

Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser

Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile 180 185 190

Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr

195 200 205

Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly 210 215 220

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Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val 260 265 270

Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile 275 280 285

Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser 290 295 300

Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met 305 310 315

Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His 325 330 335

Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro 340 345 350

Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp 355 360 365

Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser 370 380

Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr 385 390 395

Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro 405 410 415

Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn 420 425 430

Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met 435 440 445

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Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu 465 470 475 480

Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro 485 490 495

His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys 500 505

Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe 515 520 525

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- Lys Leu Gly Thr Thr Ala Ala Thr Glu Leu Lys Lys Leu Asp Phe Lys 885 890 895
- Val Ser Ser Thr Ser Asn Asn Leu Ile Ser Thr Ile Pro Ser Asp Asn 900 905 910
- Leu Ala Ala Gly Thr Asp Asn Thr Ser Ser Leu Gly Pro Pro Ser Met 915 920 925
- Pro Val His Tyr Asp Ser Gln Leu Asp Thr Thr Leu Phe Gly Lys Lys 930 935 940
- Ser Ser Pro Leu Thr Glu Ser Gly Gly Pro Leu Ser Leu Ser Glu Glu 945 950 955 960
- Asn Asn Asp Ser Lys Leu Leu Glu Ser Gly Leu Met Asn Ser Gln Glu 965 970 975
- Ser Ser Trp Gly Lys Asn Val Ser Ser Thr Glu Ser Gly Arg Leu Phe 980 985 990
- Lys Gly Lys Arg Ala His Gly Pro Ala Leu Leu Thr Lys Asp Asn Ala 995 1000 1005
- Leu Phe Lys Val Ser Ile Ser Leu Leu Lys Thr Asn Lys Thr Ser 1010 1015 1020
- Asn Asn Ser Ala Thr Asn Arg Lys Thr His Ile Asp Gly Pro Ser 1025 1030 1035
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- Lys Lys Glu Gly Pro Ile Pro Pro Asp Ala Gln Asn Pro Asp Met 1100 1105 1110
- Ser Phe Phe Lys Met Leu Phe Leu Pro Glu Ser Ala Arg Trp Ile 1115 1120 1125
- Gln Arg Thr His Gly Lys Asn Ser Leu Asn Ser Gly Gln Gly Pro 1130 1135 1140
- Ser Pro Lys Gln Leu Val Ser Leu Gly Pro Glu Lys Ser Val Glu 1145 1150 1155
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1170 .1165 1160

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| His | Thr 1235 | | Thr | Gly | Thr | Lys 1240 | | Phe | Met | Lуs | Asn 1245 | Leu | Phe | Leu |
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| Leu | Pro 1340 | | Glu | Glu | Thr | Glu 1345 | | Glu | Lys | Arg | Ile 1350 | Ile | Val | Asp |
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| Thr | Ala 1610 | | Lys | Lys | Lys | Asp 1615 | Thr | Ile | Leu | Ser | Leu 1620 | Asn | Ala | Суѕ |
| Glu | Ser 1625 | | His | Ala | Ile | Ala 1630 | Ala | Ile | Asn | Glu | Gly 1.635 | Gln | Asn | Lys |
| Pro | Glu 1640 | | Glu | Val | Thr | Trp 1645 | Ala | Lys · | Gln | Gly | Arg 1650 | Thr | Glu | Arg |
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| Asp | Asp 1685 | | Ile | e Ser | : Val | . Glu 1690 | Met | . Lys | Lys | Glu | Asp 1695 | Ph∈ | a Asp | Ile |
| Туг | Asp | | ı Asr | Glu | ı Asr | Gln 1705 | Ser | Pro | Arç | ser, | Phe 1710 | Glr | і Гля | : Lys |
| Thi | Arg 171! | | з Туі | : Phe | : Ile | Ala 1720 | Ala) | . Val | . Glu | ı Arç | Leu 1725 | Try | As <u>r</u> | Tyr |
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| Tyr | Phe 1835 | Trp | Lys | Val | Gln | His 1840 | His | Met | Ala | Pro | Thr 1845 | Ьуѕ | Asp | Glu' |
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| Lys | Asp 1865 | Val | His | Ser | Gly | Leu 1870 | | Gly | Pro | Leu | Leu 1875 | ۷al | Суѕ | His |
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| Val | Arg 1985 | | Lys | Glu | Glu | Tyr 1990 | | Met | Ala | Leu | Tyr 1995 | Asn | Leu | Tyr |
| Pro | Gly 2000 | | Phe | Glu | Thr | Val 2005 | | Met | Leu | Pro | Ser 2010 | Lys | Ala | Gly |
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| Leu | Gly 2045 | | Ala | Ser | Gly | His 2050 | Ile | Arg | J Asp | Phe | Gln 2055 | Ile | Thr | Ala |
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| Pro | Ser 2225 | | Ala | Arg | Leu | His 2230 | Leu | Gİn | Gly | Arg | Ser 2235 | Asn | Ala | Trp |
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| Gln | Lys 2255 | | Met | . Lys | Val | Thr 2260 | Gly | Val | Thr | Thr | Gln 2265 | G13 | y Val | . Lys |
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| Ası | n Ser 231 | | ı Asp | Pro | Pro | Leu 2320 | Leu) | Thr | Arg | гуг | : Leu 232 | Arç | g Ile | e His |

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ccagttggac tgattgtggg tgtgacagcc ttgggtctac taataatagg agtggtgaac 840

tgtgtcatca tgacccaggt gaaaaagaag cccttgtgcc tgcagagaga agccaaggtg

octoacttgo otgoogataa ggoooggggt acacagggoo ocgagoagoa gcacetgotg 960

atcacagege egagetecag cageagetec etggagaget eggeeagtge gttggaeaga 1020

agggegecea eteggaacea gecaeaggea eeaggegtgg aggeeagtgg ggeeggggag 1080

gecegggeca geacegggag etcagattet teceetggtg gecatgggae ecaggteaat 1140

gtcacctgca tcgtgaacgt ctgtagcagc tctgaccaca gctcacagtg ctcctcccaa 1200

gecageteca caatgggaga cacagattee ageceetegg agteeeegaa ygacgagcay 1260

gteceettet ecaaggagga atgtgeettt eggteaeage tggagaegee agagaeeetg 1320

ctggggagca ccgaagagaa gcccctgccc cttggagtgc ctgatgctgg gatgaagccc 1380

agttaaccag geeggtgtgg getgtgtegt agecaaggtg ggetgageee tggeaggatg 1440

accetgegaa ggggccetgg teettecagg c 1471

<210> 32

<211> 461

<212> PRT

<213> Homo sapiens

<400> 32

Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu
1 5 10 15

Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr 20 25 30

Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln 35 40 45

Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys 50 55 60

Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp 65 70 75 80

Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys 85 90 95

Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg 100 105 110

Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu 115 120 125

Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg

Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val 145 150 155

Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr 165 170 175

Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly 180 185 190

Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser 195 200 205

Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser

Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser : 235 230

Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly 250 245

Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly

Leu Leu Ile Ile Gly Val Val Asn Cys Val Ile Met Thr Gln Val Lys

Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro 295

Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu 315

Ile Thr Ala Pro Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser 330 325

Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly 345 340

Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser 360

Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile 375 370

Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln 395

Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro

Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser 425

Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro

Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser 455 450

<210> 33

<211> 1475

<212> DNA

<213> Homo sapiens

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tegtgagega etecaaagge ageaatgaac tteateaagt teeategaac tgtgaetgte 180

taaatggagg aacatgtgtg tccaacaagt acttctccaa cattcactgg tgcaactgcc 240

caaagaaatt cggagggcag cactgtgaaa tagataagtc aaaaacctgc tatgagggga 300

atggtcactt ttaccgagga aaggccagca ctgacaccat gggccggccc tgcctgccct 360

ggaactetge caetgteett cagcaaacgt accatgeeca cagatetgat getetteage 420

tgggcctggg gaaacataat tactgcagga acccagacaa ccggaggcga ccctggtgct 480

atgtgcaggt gggcctaaag ccgcttgtcc aagagtgcat ggtgcatgac tgcgcagatg 540

gaaaaaagcc ctcctctcct ccagaagaat taaaatttca gtgtggccaa aagactctga 600

ggccccgctt taagattatt gggggagaat tcaccaccat cgagaaccag ccctggtttg

cggccatcta caggaggcac cgggggggct ctgtcaccta cgtgtgtgga ggcagcctca 720

tcagcccttg ctgggtgatc agcgccacac actgcttcat tgattaccca aagaaggagg 780

actacatcgt ctacctgggt cgctcaaggc ttaactccaa cacgcaaggg gagatgaagt 840

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acttettace etggateege agteacacea aggaagagaa tggeetggee etetgagggt 1380

ccccagggag gaaacgggca ccacccgctt tcttgctggt tgtcattttt gcagtagagt

catetecate agetgtaaga agagaetggg aagat 1475

<210> 34

<211> 431

<212> PRT

<213> Homo sapiens

<400> 34

Met Arg Ala Leu Leu Ala Arg Leu Leu Cys Val Leu Val Val Ser

Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp 25

Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile

His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile

Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly

Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser 85

Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu 105

Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg 115

Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln 135

Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro 155 150

Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg 165

Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp 185

Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val 195

Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His 215

Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly 235 230

Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val 245

Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His

265

His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys

Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr 295

Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys 315

Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val

Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly 345

Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys 360

Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu 375 370

Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys 390

Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu

Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu 425 420

<210> 35

<211> 107

<212> PRT

<213> Mus musculus

<400> 35

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile

Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

<210> 36 <211> 120 <212> PRT

<213> Mus musculus

<400> 36 .

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 40

Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln 105 100

Gly Thr Leu Val Thr Val Ser Ser 115

<210> 37

<211> 120

<212> PRT

<213> Mus musculus

<400> 37

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser

Gly Met Ser Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Ala Leu Glu

Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp Tyr Asn Pro Ser

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val

Val Leu Lys Val Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr

Cys Ala Arg Ser Met Ile Thr Asn Trp Tyr Phe Asp Val Trp Gly Ala

Gly Thr Thr Val Thr Val Ser Ser 120

<210> 38

<211> 106

<212> PRT

WO 2004/099231

<213> Mus musculus

<400> 38

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly 10

Asp Arg Val Thr Ile Thr Cys Lys Cys Gln Leu Ser Val Gly Tyr Met 25

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr 35

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp

Asp Phe Ala Thr Tyr Tyr Cys Phe Gln Gly Ser Gly Tyr Pro Phe Thr

Phe Gly Gly Thr Lys Leu Glu Ile Lys

<210> 39

<211> 1039

<212> DNA

<213> Homo sapiens

<400> 39

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ttttctttaa gcagcaaaag gagaaaattg tcatcaaagg atattccaga ttcttgacag 120

cattctcgtc atctctgagg acatcaccat catctcagga tgaggggcat gaagctgctg

ggggcgctgc tggcactggc ggccctactg cagggggccg tgtccctgaa gatcgcagcc 240

ttcaacatcc agacatttgg ggagaccaag atgtccaatg ccaccctcgt cagctacatt

gtgcagatcc tgagccgcta tgacatcgcc ctggtccagg aggtcagaga cagccacctg

actgeegtgg ggaagetget ggacaacete aatcaggatg caccagacae etateactae 420

gtggtcagtg agccactggg acggaacagc tataaggagc gctacctgtt cgtgtacagg

cctgaccagg tgtctgcggt ggacagctac tactacgatg atggctgcga gccctgcggg

aacgacacct tcaaccgaga gccagccatt gtcaggttct tctcccggtt cacagaggtc 600

agggagtttg ccattgttcc cctgcatgcg gccccggggg acgcagtagc cgagatcgac

gctctctatg acgtctacct ggatgtccaa gagaaatggg gcttggagga cgtcatgttg

atgggcgact tcaatgcggg ctgcagctat gtgagaccct cccagtggtc atccatccgc

ctgtggacaa gccccacctt ccagtggctg atccccgaca gcgctgacac cacagctaca 840

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gttcccgact cggctcttcc ctttaacttc caggctgcct atggcctgag tgaccaactg

geccaageca teagtgacea etatecagtg gaggtgatge tgaagtgage ageceeteee 1020

cacaccagtt gaactgcag 1039

<210> 40

<211> 282

<212> PRT

<213> Homo sapiens

<400> 40

Met Arg Gly Met Lys Leu Leu Gly Ala Leu Leu Ala Leu Ala Leu 10

Leu Gln Gly Ala Val Ser Leu Lys Ile Ala Ala Phe Asn Ile Gln Thr 25 20

Phe Gly Glu Thr Lys Met Ser Asn Ala Thr Leu Val Ser Tyr Ile Val

Gln Ile Leu Ser Arg Tyr Asp Ile Ala Leu Val Gln Glu Val Arg Asp 55

Ser His Leu Thr Ala Val Gly Lys Leu Leu Asp Asn Leu Asn Gln Asp 75 70

Ala Pro Asp Thr Tyr His Tyr Val Val Ser Glu Pro Leu Gly Arg Asn

Ser Tyr Lys Glu Arg Tyr Leu Phe Val Tyr Arg Pro Asp Gln Val Ser 110 100

Ala Val Asp Ser Tyr Tyr Asp Asp Gly Cys Glu Pro Cys Gly Asn 120 115

Asp Thr Phe Asn Arg Glu Pro Ala Ile Val Arg Phe Phe Ser Arg Phe 135

Thr Glu Val Arg Glu Phe Ala Ile Val Pro Leu His Ala Ala Pro Gly 160 145 150

Asp Ala Val Ala Glu Ile Asp Ala Leu Tyr Asp Val Tyr Leu Asp Val

170 165

Gln Glu Lys Trp Gly Leu Glu Asp Val Met Leu Met Gly Asp Phe Asn

Ala Gly Cys Ser Tyr Val Arg Pro Ser Gln Trp Ser Ser Ile Arg Leu

Trp Thr Ser Pro Thr Phe Gln Trp Leu Ile Pro Asp Ser Ala Asp Thr 215

Thr Ala Thr Pro Thr His Cys Ala Tyr Asp Arg Ile Val Val Ala Gly 235 225

Met Leu Leu Arg Gly Ala Val Val Pro Asp Ser Ala Leu Pro Phe Asn 250 245

Phe Gln Ala Ala Tyr Gly Leu Ser Asp Gln Leu Ala Gln Ala Ile Ser 265

Asp His Tyr Pro Val Glu Val Met Leu Lys 280 275 .

<210> 41

<211> 678

<212> DNA

<213> Mus musculus

<400> 41

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aatggttctc caaggcttct cataaagtat gcttctgagt ctatgtctgg gatcccttcc 180

aggtttagtg gcagtggatc agggacagat tttactctta gcatcaacac tgtggagtct

gaagatattg cagattatta ctgtcaacaa agtcatagct ggccattcac gttcggctcg

gggacaaatt tggaagtaaa agaagtgaag cttgaggagt ctggaggagg cttggtgcaa 360

cctggaggat ccatgaaact ctcctgtgtt gcctctggat tcattttcag taaccactgg

atgaactggg teegeeagte teeagagaag gggettgagt gggttgetga aattagatea 480

aaatctatta attctgcaac acattatgcg gagtctgtga aagggaggtt caccatctca

agagatgatt ccaaaagtgc tgtctacctg caaatgaccg acttaagaac tgaagacact

ggegtttatt actgttccag gaattactac ggtagtacct acgaetactg gggccaaggc 660

accactctca cagtctcc 678

<210> 42

<211> 226

<212> PRT

<213> Mus musculus

<400> 42

Asp Ile Leu Leu Thr Gln Ser Pro Ala Ile Leu Ser Val Ser Pro Gly 10

Glu Arg Val Ser Phe Ser Cys Arg Ala Ser Gln Phe Val Gly Ser Ser 25

Ile His Trp Tyr Gln Gln Arg Thr Asn Gly Ser Pro Arg Leu Leu Ile

Lys Tyr Ala Ser Glu Ser Met Ser Gly Ile Pro Ser Arg Phe Ser Gly 55

Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn Thr Val Glu Ser 70 65

Glu Asp Ile Ala Asp Tyr Tyr Cys Gln Gln Ser His Ser Trp Pro Phe

Thr Phe Gly Ser Gly Thr Asn Leu Glu Val Lys Glu Val Lys Leu Glu

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Met Lys Leu Ser 115

Cys Val Ala Ser Gly Phe Ile Phe Ser Asn His Trp Met Asn Trp Val 135

Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val Ala Glu Ile Arg Ser

Lys Ser Ile Asn Ser Ala Thr His Tyr Ala Glu Ser Val Lys Gly Arg 170 165

Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ala Val Tyr Leu Gln Met 185

Thr Asp Leu Arg Thr Glu Asp Thr Gly Val Tyr Tyr Cys Ser Arg Asn 195

Tyr Tyr Gly Ser Thr Tyr Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr 215 210

Val Ser 225

<210> 43

450 <211>

<212> DNA

<213> Homo sapiens

<400> 43

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geotectgee cetgetggeg etgetggeee tetggggace tgacecagee geageetttg

tgaaccaaca cctgtgcggc tcacacctgg tggaagctct ctacctagtg tgcggggaac

gaggettett etacacacec aagaceegee gggaggeaga ggaeetgeag gtggggeagg

tggagctggg cgggggccct ggtgcaggca gcctgcagcc cttggccctg gaggggtccc

tgcagaageg tggcattgtg gaacaatget gtaccageat etgeteeete taccagetgg

agaactactg caactagacg cagecegeag geageceece accegeegee teetgeaceg 420

agagagatgg aataaagccc ttgaaccagc 450

<210> 44

110 <211>

<212> PRT

<213> Homo sapiens

<400> 44

Met Ala Leu Trp Met Arg Leu Leu Pro Leu Leu Ala Leu Leu Ala Leu

Trp Gly Pro Asp Pro Ala Ala Ala Phe Val Asn Gln His Leu Cys Gly 20

Ser His Leu Val Glu Ala Leu Tyr Leu Val Cys Gly Glu Arg Gly Phe

Phe Tyr Thr Pro Lys Thr Arg Arg Glu Ala Glu Asp Leu Gln Val Gly

Gln Val Glu Leu Gly Gly Gly Pro Gly Ala Gly Ser Leu Gln Pro Leu 65

Ala Leu Glu Gly Ser Leu Gln Lys Arg Gly Ile Val Glu Gln Cys Cys 90

Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn 110 100

45 <210>

1203 <211>

<212> DNA

Hepatitis B virus <213>

<400> 45

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ccagattggg acttcaaccc caacaaggat cactggccag aggcaatcaa ggtaggagcg 180

ggagacttcg ggccagggtt caccccacca cacggcggtc ttttggggtg gagccctcag 240

getcagggca tattgacaac agtgccagca gegeeteete etgttteeac caateggeag 300

tcaggaagac agcctactcc catctctcca cctctaagag acagtcatcc tcaggccatg 360

cagtggaact ccacaacatt ccaccaagct ctgctagatc ccagagtgag gggcctatat 420

tttcctgctg gtggctccag ttccggaaca gtaaaccctg ttccgactac tgtctcaccc 480

atatogteaa tottotogag gaotggggac cotgoacoga acatggagag cacaacatca 540

ggattcctag gacccctgct cgtgttacag gcggggtttt tcttgttgac aagaatcctc 600

acaataccac agagtetaga etegtggtgg acttetetea attttetagg gggageacce 660

acgtgtcctg gccaaaattc gcagtcccca acctccaatc actcaccaac ctcttgtcct 720

ccaatttgtc ctggttatcg ctggatgtgt ctgcggcgtt ttatcatatt cctcttcatc 780

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teagteegtt teteetgget eagtttacta gtgccatttg tteagtggtt egeagggett 1080

tececeacty tttggettte agttatatgg atgatgtggt attgggggee aagtetgtae 1140

aacatottga gtocottttt acototatta coaattttot tttgtotttg ggtatacatt 1200

tga 1203

<210> 46

<211> 400

<212> PRT

<213> Hepatitis B virus

Met Gly Gly Trp Ser Ser Lys Pro Arg Gln Gly Met Gly Thr Asn Leu .

Ser Val Pro Asn Pro Leu Gly Phe Phe Pro Asp His Gln Leu Asp Pro

Ala Phe Gly Ala Asn Ser Asn Asn Pro Asp Trp Asp Phe Asn Pro Asn

Lys Asp His Trp Pro Glu Ala Ile Lys Val Gly Ala Gly Asp Phe Gly

Pro Gly Phe Thr Pro Pro His Gly Gly Leu Leu Gly Trp Ser Pro Gln

Ala Gln Gly Ile Leu Thr Thr Val Pro Ala Ala Pro Pro Pro Val Ser

Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro Pro Leu 105

Arg Asp Ser His Pro Gln Ala Met Gln Trp Asn Ser Thr Thr Phe His 120

Gln Ala Leu Leu Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro Ala Gly 135 130

Gly Ser Ser Ser Gly Thr Val Asn Pro Val Pro Thr Thr Val Ser Pro 155 150

Ile Ser Ser Ile Phe Ser Arg Thr Gly Asp Pro Ala Pro Asn Met Glu 170 165

Ser Thr Thr Ser Gly Phe Leu Gly Pro Leu Leu Val Leu Gln Ala Gly 185 180

Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser 200

Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Ala Pro Thr Cys Pro Gly 215 210

Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro 235

Pro Ile Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile 245

Phe Leu Phe Ile Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu

Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu Leu Pro Gly Thr Ser 280

Thr Thr Ser Thr Gly Pro Cys Lys Thr Cys Thr Ile Pro Ala Gln Gly

Thr Ser Met Phe Pro Ser Cys Cys Cys Thr Lys Pro Ser Asp Gly Asn 315 310 305

Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Ala Arg Phe Leu 330 325

Trp Glu Trp Ala Ser Val Arg Phe Ser Trp Leu Ser Leu Leu Val Pro 345 340

Phe Val Gln Trp Phe Ala Gly Leu Ser Pro Thr Val Trp Leu Ser Val 360

Ile Trp Met Met Trp Tyr Trp Gly Pro Ser Leu Tyr Asn Ile Leu Ser 380 375

Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys Leu Trp Val Tyr Ile 395 390 385

<210> 47

<211> 799

<212> DNA

<213> Homo sapiens

<400> 47

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gtecetgete etggettttg geetgetetg eetgeeetgg etteaagagg geagtgeett 120

cocaaccatt cocttatoca ggccttttga caacgctatg ctccgcgccc atcgtctgca 180

ccagctggcc tttgacacct accaggagtt tgaagaagcc tatatcccaa aggaacagaa

gtattcattc ctgcagaacc cccagacctc cctctgtttc tcagagtcta ttccgacacc 300

ctccaacagg gaggaaacac aacagaaatc caacctagag ctgctccgca tctccctgct 360

geteatecag tegtggetgg agecegtgea gtteeteagg agtgtetteg eeaacageet

ggtgtacggc gcctctgaca gcaacgtcta tgacctccta aaggacctag aggaaggcat 480

ccaaacgctg atggggaggc tggaagatgg cagcccccgg actgggcaga tcttcaagca

gacctacage aagttegaca caaacteaca caacgatgae geactactea agaactaegg 600

getgetetae tgetteagga aggaeatgga caaggtegag acatteetge geategtgea 660

gtgccgctct gtggagggca gctgtggctt ctagctgccc gggtggcatc cctgtgaccc

etecceagtg ceteteetgg ceetggaagt tgccactcca gtgcccacca gccttgtcct

aataaaatta agttgcatc 799

<210> 48

<211> 217

<212> PRT

<213> Homo sapiens

<400> 48

Met Ala Thr Gly Ser Arg Thr Ser Leu Leu Leu Ala Phe Gly Leu Leu 10

Cys Leu Pro Trp Leu Gln Glu Gly Ser Ala Phe Pro Thr Ile Pro Leu 25

Ser Arg Pro Phe Asp Asn Ala Met Leu Arg Ala His Arg Leu His Gln

Leu Ala Phe Asp Thr Tyr Gln Glu Phe Glu Glu Ala Tyr Ile Pro Lys 55

Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro Gln Thr Ser Leu Cys Phe

Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg Glu Glu Thr Gln Gln Lys 90

Ser Asn Leu Glu Leu Leu Arg Ile Ser Leu Leu Leu Ile Gln Ser Trp 105

Leu Glu Pro Val Gln Phe Leu Arg Ser Val Phe Ala Asn Ser Leu Val 125 120 115

Tyr Gly Ala Ser Asp Ser Asn Val Tyr Asp Leu Leu Lys Asp Leu Glu 135

Glu Gly Ile Gln Thr Leu Met Gly Arg Leu Glu Asp Gly Ser Pro Arg 155 150

Thr Gly Gln Ile Phe Lys Gln Thr Tyr Ser Lys Phe Asp Thr Asn Ser 170 165

His Asn Asp Asp Ala Leu Leu Lys Asn Tyr Gly Leu Leu Tyr Cys Phe 185

Arg Lys Asp Met Asp Lys Val Glu Thr Phe Leu Arg Ile Val Gln Cys 195

Arg Ser Val Glu Gly Ser Cys Gly Phe 210

49 <210>

<211> 963

<212> DNA

<213> Homo sapiens

<400> 49

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Gln Glu Ser Val Gly Ala Gly Ala Gly Glu Ala Ala Val Asp Lys Thr 85 90 95

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser 100 105 110

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Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80

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Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

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Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe 50 60

Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr 65 70 75 80

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Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr Thr Ala Tyr 70 75 80

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aatgagccag accaccacga ctttgacaac gtctccatga ccatgcaagg cttcctgaac 600

tactacgatg cctgctcgga gggtctgcgc gccgccagcc ccgccctgcg gctgggaggc 660

cccggcgact ccttccacac cccaccgcga tccccgctga gctggggcct cctgcgccac 720

tgccacgacg gtaccaactt cttcactggg gaggcgggcg tgcggctgga ctacatctcc 780

ctccacagga agggtgcgcg cagctccatc tccatcctgg agcaggagaa ggtcgtcgcg 840

cagcagatec ggcagetett ecceaagtte geggaeacec ecatttacaa egaegaggeg 900

gaccegetgg tgggctggtc cetgccacag cegtggaggg eggaegtgae etaegeggee 960

atggtggtga aggtcatcgc gcagcatcag aacctgctac tggccaacac cacctccgcc 1020

ttcccctacg cgctcctgag caacgacaat gccttcctga gctaccaccc gcaccccttc 1080

gegeagegea egeteacege gegettecag gteaacaaca ecegeeegee geaegtgeag

ctgttgcgca agccggtgct cacggccatg gggctgctgg cgctgctgga tgaggagcag 1200

ctctgggccg aagtgtcgca ggccgggacc gtcctggaca gcaaccacac ggtgggcgtc 1260

86

ctggccageg cccacegece ccagggeceg geogaegect ggegegeege ggtgctgate 1320

tacgcgageg acgacaccc cgcccacccc aaccgcageg tegeggtgac cetgeggetg 1380

cgcggggtgc cccccggccc gggcctggtc tacgtcacgc gctacctgga caacgggctc 1440

tgcagccccg acggcgagtg gcggccctg ggccggcccg tettccccac.ggcagagcag 1500

ggcggccgcc tgaccctgcg ccccgcgctg cggctgccgt cgcttttgct ggtgcacgtg 1620

tgtgcgcgcc ccgagaagcc gcccgggcag gtcacgcggc tccgcgccct gcccctgacc 1680

caagggcage tggttetggt etggteggat gaacaegtgg getecaagtg eetgtggaca 1740

tacgagatec agttetetea ggaeggtaag gegtaeacee eggteageag gaageeateg 1800

acettcaace tetttgtgtt cageccagae acaggtgetg tetetggete etacegagtt 1860

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<210> 66

<211> 653

<212> PRT

<213> Homo sapiens

<400> 66

Met Arg Pro Leu Arg Pro Arg Ala Ala Leu Leu Ala Leu Leu Ala Ser 1 5 10 15

Leu Leu Ala Ala Pro Pro Val Ala Pro Ala Glu Ala Pro His Leu Val 20 25 30

Gln Val Asp Ala Ala Arg Ala Leu Trp Pro Leu Arg Arg Phe Trp Arg 35 40 45

Ser Thr Gly Phe Cys Pro Pro Leu Pro His Ser Gln Ala Asp Gln Tyr 50 55 60

Val Leu Ser Trp Asp Gln Gln Leu Asn Leu Ala Tyr Val Gly Ala Val 65 70 75 80

Pro His Arg Gly Ile Lys Gln Val Arg Thr His Trp Leu Leu Glu Leu 85 90 95

Val Thr Thr Arg Gly Ser Thr Gly Arg Gly Leu Ser Tyr Asn Phe Thr

WO 2004/099231 105 110 His Leu Asp Gly Tyr Leu Asp Leu Leu Arg Glu Asn Gln Leu Leu Pro 120 115 Gly Phe Glu Leu Met Gly Ser Ala Ser Gly His Phe Thr Asp Phe Glu 135 Asp Lys Gln Gln Val Phe Glu Trp Lys Asp Leu Val Ser Ser Leu Ala 155 Arg Arg Tyr Ile Gly Arg Tyr Gly Leu Ala His Val Ser Lys Trp Asn Phe Glu Thr Trp Asn Glu Pro Asp His His Asp Phe Asp Asn Val Ser 185 180 Met Thr Met Gln Gly Phe Leu Asn Tyr Tyr Asp Ala Cys Ser Glu Gly 200 Leu Arg Ala Ala Ser Pro Ala Leu Arg Leu Gly Gly Pro Gly Asp Ser 210 215 Phe His Thr Pro Pro Arg Ser Pro Leu Ser Trp Gly Leu Leu Arg His 230 Cys His Asp Gly Thr Asn Phe Phe Thr Gly Glu Ala Gly Val Arg Leu Asp Tyr Ile Ser Leu His Arg Lys Gly Ala Arg Ser Ser Ile Ser Ile 265 260

Leu Glu Gln Glu Lys Val Val Ala Gln Gln Ile Arg Gln Leu Phe Pro

Lys Phe Ala Asp Thr Pro Ile Tyr Asn Asp Glu Ala Asp Pro Leu Val 290

Gly Trp Ser Leu Pro Gln Pro Trp Arg Ala Asp Val Thr Tyr Ala Ala 310

Met Val Val Lys Val Ile Ala Gln His Gln Asn Leu Leu Ala Asn 325

Thr Thr Ser Ala Phe Pro Tyr Ala Leu Leu Ser Asn Asp Asn Ala Phe 340

Leu Ser Tyr His Pro His Pro Phe Ala Gln Arg Thr Leu Thr Ala Arg 360

Phe Gln Val Asn Asn Thr Arg Pro Pro His Val Gln Leu Leu Arg Lys 375 370

Pro Val Leu Thr Ala Met Gly Leu Leu Ala Leu Leu Asp Glu Glu Gln 395 390

Leu Trp Ala Glu Val Ser Gln Ala Gly Thr Val Leu Asp Ser Asn His 410 405

Thr Val Gly Val Leu Ala Ser Ala His Arg Pro Gln Gly Pro Ala Asp 425 420

Ala Trp Arg Ala Ala Val Leu Ile Tyr Ala Ser Asp Asp Thr Arg Ala 435 440 445

His Pro Asn Arg Ser Val Ala Val Thr Leu Arg Leu Arg Gly Val Pro 450 455 460

Pro Gly Pro Gly Leu Val Tyr Val Thr Arg Tyr Leu Asp Asn Gly Leu 465 470 475 480

Cys Ser Pro Asp Gly Glu Trp Arg Arg Leu Gly Arg Pro Val Phe Pro 485 490 495

Thr Ala Glu Gln Phe Arg Arg Met Arg Ala Ala Glu Asp Pro Val Ala 500 505 510

Ala Ala Pro Arg Pro Leu Pro Ala Gly Gly Arg Leu Thr Leu Arg Pro 515 520 525

Ala Leu Arg Leu Pro Ser Leu Leu Leu Val His Val Cys Ala Arg Pro 530 540

Glu Lys Pro Pro Gly Gln Val Thr Arg Leu Arg Ala Leu Pro Leu Thr 545 550 555 560

Gln Gly Gln Leu Val Leu Val Trp Ser Asp Glu His Val Gly Ser Lys 565 570 575

Cys Leu Trp Thr Tyr Glu Ile Gln Phe Ser Gln Asp Gly Lys Ala Tyr 580 585 590

Thr Pro Val Ser Arg Lys Pro Ser Thr Phe Asn Leu Phe Val Phe Ser 595 600 605

Pro Asp Thr Gly Ala Val Ser Gly Ser Tyr Arg Val Arg Ala Leu Asp

Tyr Trp Ala Arg Pro Gly Pro Phe Ser Asp Pro Val Pro Tyr Leu Glu 625 630 635 640

Val Pro Val Pro Arg Gly Pro Pro Ser Pro Gly Asn Pro 645 650

<210> 67

<211> 1290

<212> DNA

<213> Homo sapiens

<400> 67

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accatgggct ggctgcactg ggagcgcttc atgtgcaacc ttgactgcca ggaagagcca 180

gattcctgca tcagtgagaa gctcttcatg gagatggcag agctcatggt ctcagaaggc 240

tggaaggatg caggttatga gtacctctgc attgatgact gttggatggc tccccaaaga 300

gattcagaag gcagacttca ggcagaccct cagcgctttc ctcatgggat tcgccagcta 360

gctaattatg ttcacagcaa aggactgaag ctagggattt atgcagatgt tggaaataaa 420

acctgcgcag gcttccctgg gagttttgga tactacgaca ttgatgccca gacctttgct 480

gactggggag tagatctgct aaaatttgat ggttgttact gtgacagttt ggaaaatttg 540

gcagatggtt ataagcacat gtccttggcc ctgaatagga ctggcagaag cattgtgtac 600

toctgtgagt ggcctcttta tatgtggccc tttcaaaagc ccaattatac agaaatccga

cagtactgca atcactggcg aaattttgct gacattgatg attcctggaa aagtataaag 720

agtatcttgg actggacatc ttttaaccag gagagaattg ttgatgttgc tggaccaggg 780

ggttggaatg acccagatat gttagtgatt ggcaactttg gcctcagctg gaatcagcaa 840

gtaactcaga tggccctctg ggctatcatg gctgctcctt tattcatgtc taatgacctc

cgacacatca gccctcaagc caaagctctc cttcaggata aggacgtaat tgccatcaat 960

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gaacgacctc tctcaggctt agcctgggct gtagctatga taaaccggca ggagattggt 1080

ggacctcgct cttataccat cgcagttgct tccctgggta aaggagtggc ctgtaatcct 1140

gcctgcttca tcacacagct cctccctgtg aaaaggaagc tagggttcta tgaatggact 1200

tcaaggttaa gaagtcacat aaatcccaca ggcactgttt tgcttcagct agaaaataca 1260

atgcagatgt cattaaaaga cttactttaa 1290

<210> 68

<211> 429

<212> PRT

<213> Homo sapiens

<400> 68

Met Gln Leu Arg Asn Pro Glu Leu His Leu Gly Cys Ala Leu Ala Leu

Arg Phe Leu Ala Leu Val Ser Trp Asp Ile Pro Gly Ala Arg Ala Leu 20 25 30

Asp Asn Gly Leu Ala Arg Thr Pro Thr Met Gly Trp Leu His Trp Glu 35 40 45

Arg Phe Met Cys Asn Leu Asp Cys Gln Glu Glu Pro Asp Ser Cys Ile 50 55 60

Ser Glu Lys Leu Phe Met Glu Met Ala Glu Leu Met Val Ser Glu Gly 65 70 75 80

Trp Lys Asp Ala Gly Tyr Glu Tyr Leu Cys Ile Asp Asp Cys Trp Met 85 90 95

Ala Pro Gln Arg Asp Ser Glu Gly Arg Leu Gln Ala Asp Pro Gln Arg 100 105 110

Phe Pro His Gly Ile Arg Gln Leu Ala Asn Tyr Val His Ser Lys Gly 115 120 125

Leu Lys Leu Gly Ile Tyr Ala Asp Val Gly Asn Lys Thr Cys Ala Gly 130 135 140

Phe Pro Gly Ser Phe Gly Tyr Tyr Asp Ile Asp Ala Gln Thr Phe Ala 145 150 155 160

Asp Trp Gly Val Asp Leu Leu Lys Phe Asp Gly Cys Tyr Cys Asp Ser 165 170 175.

Leu Glu Asn Leu Ala Asp Gly Tyr Lys His Met Ser Leu Ala Leu Asn 180 185 190

Arg Thr Gly Arg Ser Ile Val Tyr Ser Cys Glu Trp Pro Leu Tyr Met
195 200 205

Trp Pro Phe Gln Lys Pro Asn Tyr Thr Glu Ile Arg Gln Tyr Cys Asn 210 215 220

His Trp Arg Asn Phe Ala Asp Ile Asp Asp Ser Trp Lys Ser Ile Lys 225 230 235 240

Ser Ile Leu Asp Trp Thr Ser Phe Asn Gln Glu Arg Ile Val Asp Val 245 250 255

Ala Gly Pro Gly Gly Trp Asn Asp Pro Asp Met Leu Val Ile Gly Asn 260 265 270

Phe Gly Leu Ser Trp Asn Gln Gln Val Thr Gln Met Ala Leu Trp Ala 275 280 285

Ile Met Ala Ala Pro Leu Phe Met Ser Asn Asp Leu Arg His Ile Ser 290 295 300

Pro Gln Ala Lys Ala Leu Leu Gln Asp Lys Asp Val Ile Ala Ile Asn 305 310 315

Gln Asp Pro Leu Gly Lys Gln Gly Tyr Gln Leu Arg Gln Gly Asp Asn 325 330 335

Phe Glu Val Trp Glu Arg Pro Leu Ser Gly Leu Ala Trp Ala Val Ala 340 345 350

Met Ile Asn Arg Gln Glu Ile Gly Gly Pro Arg Ser Tyr Thr Ile Ala 355 360 365

Val Ala Ser Leu Gly Lys Gly Val Ala Cys Asn Pro Ala Cys Phe Ile 370 375 380

Thr Gln Leu Leu Pro Val Lys Arg Lys Leu Gly Phe Tyr Glu Trp Thr 385 390 395 400

Ser Arg Leu Arg Ser His Ile Asn Pro Thr Gly Thr Val Leu Leu Gln 405 410 415

Leu Glu Asn Thr Met Gln Met Ser Leu Lys Asp Leu Leu
420 425

<210> 69

<211> 351

<212> DNA

<213> Homo sapiens

<400> 69

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ttcttctccc agccgggtgc cccaatactt cagtgcatgg gctgctgctt ctctagagca 180

tateceacte cactaaggte caagaagaeg atgttggtee aaaagaaegt caceteagag

tocacttgct gtgtagctaa atcatataac agggtcacag taatgggggg tttcaaagtg 300

gagaaccaca cggcgtgcca ctgcagtact tgttattatc acaaatctta a 351 .

<210> 70

<211> 116

<212> PRT

<213> Homo sapiens

<400> 70

Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser 1 5 10 15

Val Phe Leu His Val Leu His Ser Ala Pro Asp Val Gln Asp Cys Pro 20 25 30

Glu Cys Thr Leu Gln Glu Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro 35 40 45

Ile Leu Gln Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro 50 60

Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn Val Thr Ser Glu 65 70 75 80

Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly 85 90 95

Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr 100 105 110

Tyr His Lys Ser 115

<210> 71

<211> 498

<212> DNA

<213> Homo sapiens

<400> 71

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tecaaggage egetteggee acggtgeege cecateaatg ceaccetgge tgtggagaag 120

gagggetgee cegtgtgeat cacegteaac accaecatet gtgeeggeta etgeeceaec 180

atgaccegeg tgetgcaggg ggtcctgccg gccctgcctc aggtggtgtg caactaccgc

gatgtgcdct tcgagtccat ccggctccct ggctgcccgc gcggcgtgaa ccccgtggtc 300

tectacgeeg tggeteteag etgteaatgt geactetgee geegeageae eactgaetge 360

gggggtccca aggaccaccc cttgacctgt gatgaccccc gcttccagga ctcctcttcc 420

tcaaaggccc ctcccccag ccttccaagc ccatcccgac tcccggggcc ctcggacacc 480

ccgatcctcc cacaataa 498

<210> 72

<211> 165

<212> PRT

<213> Homo sapiens

<400> 72

Met Glu Met Phe Gln Gly Leu Leu Leu Leu Leu Leu Leu Ser Met Gly
1 10 15

Gly Thr Trp Ala Ser Lys Glu Pro Leu Arg Pro Arg Cys Arg Pro Ile 20 25 30

Asn Ala Thr Leu Ala Val Glu Lys Glu Gly Cys Pro Val Cys Ile Thr 35 40 45

Val Asn Thr Thr Ile Cys Ala Gly Tyr Cys Pro Thr Met Thr Arg Val

50 55

Leu Gln Gly Val Leu Pro Ala Leu Pro Gln Val Val Cys Asn Tyr Arg 65 70 75 80

Asp Val Arg Phe Glu Ser Ile Arg Leu Pro Gly Cys Pro Arg Gly Val 85 90 95

Asn Pro Val Val Ser Tyr Ala Val Ala Leu Ser Cys Gln Cys Ala Leu 100 105 110

Cys Arg Arg Ser Thr Thr Asp Cys Gly Gly Pro Lys Asp His Pro Leu 115 120 125

Thr Cys Asp Asp Pro Arg Phe Gln Asp Ser Ser Ser Ser Lys Ala Pro 130 135 140

Pro Pro Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr 145 150 155 160

Pro Ile Leu Pro Gln 165

<210> 73

<211> 165

<212> PRT

<213> Homo sapiens

Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His

Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe 35 40 45

Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val Trp 50 55 60

Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu 65 70 75 80

Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp 85 90 95

Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu 100 105 110

Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala 115 120 125

Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val 130 135 140

Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala 145 150 150

Cys Arg Thr Gly Asp 165 <210> 74

<211> 588

<212> DNA

<213> Homo sapiens

<400> 74

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ctgcaccaaa tgaggagaat ctcccctttc ttgtgtctca aggacagaag agacttcagg 180

ttcccccagg agatggtaaa agggagccag ttgcagaagg cccatgtcat gtctgtcctc 240

catgagatge tgcagcagat cttcagcete ttccacacag agegeteete tgctgcctgg 300

aacatgaccc tectagacca actecacact ggaetteate ageaactgea acacetggag 360

acctgcttgc tgcaggtagt gggagaagga gaatctgctg gggcaattag cagccctgca 420

ctgaccttga ggaggtactt ccagggaatc cgtgtctacc tgaaagagaa gaaatacagc 480

gactgtgcct gggaagttgt cagaatggaa atcatgaaat ccttgttctt atcaacaaac 540

atgcaagaaa gactgagaag taaagataga gacctgggct catcttga 588

<210> 75

<211> 195

<212> PRT

<213> Homo sapiens

<400> 75

Met Ala Leu Leu Phe Pro Leu Leu Ala Ala Leu Val Met Thr Ser Tyr
1 5 10 15

Ser Pro Val Gly Ser Leu Gly Cys Asp Leu Pro Gln Asn His Gly Leu 20 25 30

Leu Ser Arg Asn Thr Leu Val Leu Leu His Gln Met Arg Arg Ile Ser 35 40 45

Pro Phe Leu Cys Leu Lys Asp Arg Arg Asp Phe Arg Phe Pro Gln Glu 50 . 55 60

Met Val Lys Gly Ser Gln Leu Gln Lys Ala His Val Met Ser Val Leu 65 70 75 80

His Glu Met Leu Gln Gln Ile Phe Ser Leu Phe His Thr Glu Arg Ser 85 90 95

Ser Ala Ala Trp Asn Met Thr Leu Leu Asp Gln Leu His Thr Gly Leu 100 105 . 110

His Gln Gln Leu Gln His Leu Glu Thr Cys Leu Leu Gln Val Val Gly 115 120 125

Glu Gly Glu Ser Ala Gly Ala Ile Ser Ser Pro Ala Leu Thr Leu Arg 130 135 140

Arg Tyr Phe Gln Gly Ile Arg Val Tyr Leu Lys Glu Lys Lys Tyr Ser 145 150 155

Asp Cys Ala Trp Glu Val Val Arg Met Glu Ile Met Lys Ser Leu Phe 165 170 175

Leu Ser Thr Asn Met Gln Glu Arg Leu Arg Ser Lys Asp Arg Asp Leu 180 185 190

Gly Ser Ser 195

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